



Clinical trial results:

A dose finding study to assess the safety and efficacy of K-877 in patients with statin-controlled LDL-C but abnormal lipid levels

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2013-001517-32 |
| Trial protocol | SE GB HU DE CZ NL DK PL |
| Global end of trial date | 23 September 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 01 April 2016 |
| First version publication date | 01 April 2016 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | K-877-201 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Kowa Research Europe Ltd |
| Sponsor organisation address | 105 Wharfedale Road, Winnersh Triangle, Wokingham, United Kingdom, RG41 5RB |
| Public contact | Regulatory Affairs, Kowa Research Europe Ltd, +44 0118 922 9000, |
| Scientific contact | Regulatory Affairs, Kowa Research Europe Ltd, +44 0118 922 9000, |

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 | 20 October 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 September 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 September 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the dose response of the following parameters:

- % change in non-high-density lipoprotein cholesterol (non-HDL-C) from baseline to Week 12
- % change in TG from baseline to Week 12

To assess the safety and tolerability of K-877 in patients with residual cardiovascular risk despite statin-controlled low density lipoprotein (LDL-C) concentration as particularly evaluated by:

- Change and % change in serum creatinine from baseline to Week 12
- Change and % change in log(homocysteine) from baseline to Week 12

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. Each patient was assured of his/her right to withdraw from the study at any time. Close monitoring of all subjects was adhered to throughout the trial conduct.

Throughout the study, patients were not allowed to change the dose, dosing regimen (e.g. morning or evening dose), or the type of statin and encouraged to continue on the same diet and exercise regimen. In general, any other medication not excluded by the protocol was permitted.

Background therapy:

Stable statin therapy (except for pravastatin, lovastatin, and fluvastatin)

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 11 October 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Poland: 31 |
| Country: Number of subjects enrolled | Netherlands: 56 |
| Country: Number of subjects enrolled | Sweden: 19 |
| Country: Number of subjects enrolled | United Kingdom: 17 |
| Country: Number of subjects enrolled | Czech Republic: 38 |
| Country: Number of subjects enrolled | Denmark: 34 |
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Hungary: 93 |
| Country: Number of subjects enrolled | Russian Federation: 116 |
| Worldwide total number of subjects | 408 |
| EEA total number of subjects | 292 |

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) | 273 |
| From 65 to 84 years | 135 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening Period was up to a maximum of 4 weeks in duration and consisted of 1 or 2 visits: Screening Visit (SV) 1 for all patients, and SV 2 for patients who failed to meet inclusion criterion #5 (fasting TG ≥ 175 mg/dL [1.97 mmol/L] and ≤ 500 mg/dL [5.65 mmol/L]) at SV 1.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

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

Arm description: -

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two placebo tablets were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|------------------|---------------------------|
| Arm title | K-877 0.05 mg twice daily |
|------------------|---------------------------|

Arm description: -

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | K-877 0.05 mg tablet |
| Investigational medicinal product code | K-877 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One K-877 0.05 mg tablet and one placebo tablet were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|--|--------------------|
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One K-877 0.05 mg tablet and one placebo tablet were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|------------------|--------------------------|
| Arm title | K-877 0.1 mg twice daily |
|------------------|--------------------------|

Arm description: -

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|---------------------|
| Investigational medicinal product name | K-877 0.1 mg tablet |
| Investigational medicinal product code | K-877 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One K-877 0.1 mg tablet and one placebo tablet were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|--|--------------------|
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One K-877 0.1 mg tablet and one placebo tablet were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|------------------|--------------------------|
| Arm title | K-877 0.2 mg twice daily |
|------------------|--------------------------|

Arm description: -

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | K-877 0.2 mg tablet |
| Investigational medicinal product code | K-877 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One K-877 0.2 mg tablet and one placebo tablet were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|--|--------------------|
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

One K-877 0.2 mg tablet and one placebo tablet were to be taken orally, twice daily in the morning and the evening. Duration of treatment was 12 weeks.

| | |
|------------------|-------------------------|
| Arm title | K-877 0.1 mg once daily |
|------------------|-------------------------|

Arm description: -

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | K-877 0.05 mg tablet |
| Investigational medicinal product code | K-877 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two K-877 0.05 mg tablets were to be taken orally in the morning and two placebo tablets were to be taken orally in the evening. Duration of treatment was 12 weeks.

| | |
|--|--------------------|
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two K-877 0.05 mg tablets were to be taken orally in the morning and two placebo tablets were to be

taken orally in the evening. Duration of treatment was 12 weeks.

| | |
|---|-------------------------|
| Arm title | K-877 0.2 mg once daily |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | K-877 0.1 mg tablet |
| Investigational medicinal product code | K-877 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two K-877 0.1 mg tablets were to be taken orally in the morning and two placebo tablets were to be taken orally in the evening. Duration of treatment was 12 weeks. | |
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two K-877 0.1 mg tablets were to be taken orally in the morning and two placebo tablets were to be taken orally in the evening. Duration of treatment was 12 weeks. | |
| Arm title | K-877 0.4 mg once daily |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | K-877 0.2 mg tablet |
| Investigational medicinal product code | K-877 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two K-877 0.2 mg tablets were to be taken orally in the morning and two placebo tablets were to be taken orally in the evening. Duration of treatment was 12 weeks. | |
| Investigational medicinal product name | Placebo tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two K-877 0.2 mg tablets were to be taken orally in the morning and two placebo tablets were to be taken orally in the evening. Duration of treatment was 12 weeks. | |

| Number of subjects in period 1 | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily |
|---------------------------------------|---------------------|---------------------------|--------------------------|
| Started | 60 | 58 | 58 |
| Completed | 55 | 54 | 50 |
| Not completed | 5 | 4 | 8 |
| Consent withdrawn by subject | 3 | 4 | 3 |
| Adverse event, non-fatal | 1 | - | 2 |
| Lost to follow-up | - | - | 2 |
| Protocol deviation | 1 | - | 1 |

| Number of subjects in period 1 | K-877 0.2 mg twice daily | K-877 0.1 mg once daily | K-877 0.2 mg once daily |
|---------------------------------------|--------------------------|-------------------------|-------------------------|
| Started | 57 | 58 | 58 |
| Completed | 52 | 54 | 56 |
| Not completed | 5 | 4 | 2 |
| Consent withdrawn by subject | 2 | 2 | 1 |
| Adverse event, non-fatal | 3 | 2 | 1 |
| Lost to follow-up | - | - | - |
| Protocol deviation | - | - | - |

| Number of subjects in period 1 | K-877 0.4 mg once daily |
|---------------------------------------|-------------------------|
| Started | 59 |
| Completed | 54 |
| Not completed | 5 |
| Consent withdrawn by subject | 3 |
| Adverse event, non-fatal | 1 |
| Lost to follow-up | - |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------------------|
| Reporting group title | Placebo twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.05 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.1 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.2 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.1 mg once daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.2 mg once daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.4 mg once daily |
| Reporting group description: - | |

| Reporting group values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily |
|---------------------------------------|---------------------|---------------------------|--------------------------|
| Number of subjects | 60 | 58 | 58 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 38 | 39 | 40 |
| From 65-84 years | 22 | 19 | 18 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 61 | 59 | 58 |
| standard deviation | ± 10.3 | ± 9.8 | ± 12.3 |
| Gender categorical Units: Subjects | | | |
| Female | 17 | 18 | 18 |
| Male | 43 | 40 | 40 |

| Reporting group values | K-877 0.2 mg twice daily | K-877 0.1 mg once daily | K-877 0.2 mg once daily |
|---------------------------------------|--------------------------|-------------------------|-------------------------|
| Number of subjects | 57 | 58 | 58 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 37 | 43 | 37 |
| From 65-84 years | 20 | 15 | 21 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 61 | 57 | 59 |
| standard deviation | ± 8.9 | ± 9.7 | ± 11.7 |
| Gender categorical Units: Subjects | | | |
| Female | 17 | 24 | 18 |

| | | | |
|------|----|----|----|
| Male | 40 | 34 | 40 |
|------|----|----|----|

| Reporting group values | K-877 0.4 mg once daily | Total | |
|---------------------------------------|-------------------------|-------|--|
| Number of subjects | 59 | 408 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 39 | 273 | |
| From 65-84 years | 20 | 135 | |
| 85 years and over | 0 | 0 | |
| Age continuous Units: years | | | |
| arithmetic mean | 59 | | |
| standard deviation | ± 9.7 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 14 | 126 | |
| Male | 45 | 282 | |

End points

End points reporting groups

| | |
|--------------------------------|---------------------------|
| Reporting group title | Placebo twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.05 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.1 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.2 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.1 mg once daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.2 mg once daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.4 mg once daily |
| Reporting group description: - | |

Primary: Percent change in TG

| | |
|---------------------------------|----------------------|
| End point title | Percent change in TG |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 52 | 50 | 49 |
| Units: percent | | | | |
| least squares mean (standard error) | 15 (± 4.85) | -21.2 (± 4.96) | -30.8 (± 5.08) | -39.5 (± 5.11) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 52 | 52 | |
| Units: percent | | | | |
| least squares mean (standard error) | -19.1 (± 4.98) | -22.7 (± 4.88) | -27.7 (± 4.99) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -36.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -53.5 |
| upper limit | -18.7 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.72 |

| | |
|---|--|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -45.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -63.4 |
| upper limit | -28.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.81 |

| | |
|---|--|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -54.4 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -72.1 |
| upper limit | -36.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.83 |

| | |
|---|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -51.5 |
| upper limit | -16.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.76 |

| | |
|---|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -37.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -55 |
| upper limit | -20.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.72 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -42.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -60.1 |
| upper limit | -25.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.75 |

Primary: Percent change in non-HDL-C

| | |
|---------------------------------|-----------------------------|
| End point title | Percent change in non-HDL-C |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 52 | 50 | 49 |
| Units: percent | | | | |
| least squares mean (standard error) | 2.1 (± 2.9) | -4.8 (± 2.98) | -5.4 (± 3.04) | -6.8 (± 3.05) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 52 | 52 | |
| Units: percent | | | | |
| least squares mean (standard error) | -3.2 (± 2.96) | -7.1 (± 2.88) | -5.7 (± 2.99) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.307 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -6.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.8 |
| upper limit | 3.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.87 |

| | |
|---|--|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.237 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -7.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.5 |
| upper limit | 2.7 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.91 |

| | |
|---|--|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.111 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -8.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19 |
| upper limit | 1.3 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.91 |

| | |
|---|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.582 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -5.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.3 |
| upper limit | 4.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.88 |

| | |
|---|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.086 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -9.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.1 |
| upper limit | 0.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.85 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Dunnett's Test in MMRM Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.187 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -7.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.8 |
| upper limit | 2.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.87 |

Primary: Percent change in serum creatinine

| | |
|---------------------------------|------------------------------------|
| End point title | Percent change in serum creatinine |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 54 |
| Units: percent | | | | |
| least squares mean (standard error) | 1.13 (± 1.41) | 1.53 (± 1.43) | 1.82 (± 1.46) | 4.92 (± 1.46) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | 1.15 (± 1.4) | 3.02 (± 1.36) | 3.56 (± 1.43) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.824 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.19 |
| upper limit | 4.01 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.83 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.706 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.94 |
| upper limit | 4.34 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.85 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.04 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 3.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.17 |
| upper limit | 7.43 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.85 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.989 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.55 |
| upper limit | 3.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.82 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.297 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.67 |
| upper limit | 5.46 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.81 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.185 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.17 |
| upper limit | 6.05 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.84 |

Primary: Percent change in Log(Homocysteine)

| | |
|---------------------------------|-------------------------------------|
| End point title | Percent change in Log(Homocysteine) |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 54 |
| Units: percent | | | | |
| least squares mean (standard error) | 3 (± 1.14) | 2.9 (± 1.16) | 5.89 (± 1.18) | 8.45 (± 1.18) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | 3.93 (± 1.13) | 5.91 (± 1.1) | 8.37 (± 1.15) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.948 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.01 |
| upper limit | 2.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.48 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.054 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.05 |
| upper limit | 5.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.49 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 5.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.51 |
| upper limit | 8.39 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.49 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.529 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.97 |
| upper limit | 3.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.47 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.048 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.03 |
| upper limit | 5.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.47 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 5.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.46 |
| upper limit | 8.28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.48 |

Secondary: Percent change in HDL-C

| | |
|---------------------------------|-------------------------|
| End point title | Percent change in HDL-C |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 54 |
| Units: percent | | | | |
| least squares mean (standard error) | -0.05 (± 2.69) | 7.59 (± 2.73) | 12.84 (± 2.8) | 10.89 (± 2.78) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | 3.66 (± 2.66) | 10.32 (± 2.6) | 7.29 (± 2.73) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.029 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 7.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 14.53 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.5 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 12.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.94 |
| upper limit | 19.84 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.53 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 10.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.01 |
| upper limit | 17.88 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.53 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.286 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 3.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.12 |
| upper limit | 10.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.48 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 10.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.55 |
| upper limit | 17.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.47 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.036 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 7.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 14.22 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.5 |

Secondary: Percent change in total cholesterol

| | |
|---------------------------------|-------------------------------------|
| End point title | Percent change in total cholesterol |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 54 |
| Units: percent | | | | |
| least squares mean (standard error) | 0.65 (± 2.1) | -1.42 (± 2.12) | -1.99 (± 2.17) | -3.13 (± 2.17) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | -1.67 (± 2.07) | -2.12 (± 2.02) | -1.68 (± 2.12) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.446 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.43 |
| upper limit | 3.28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.72 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.338 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.05 |
| upper limit | 2.77 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.75 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.169 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -3.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.19 |
| upper limit | 1.62 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.75 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.392 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.64 |
| upper limit | 3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.71 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.306 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.07 |
| upper limit | 2.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.7 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.393 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.68 |
| upper limit | 3.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.72 |

Secondary: Percent change in Remnant Cholesterol

| | |
|---------------------------------|---------------------------------------|
| End point title | Percent change in Remnant Cholesterol |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 54 |
| Units: percent | | | | |
| least squares mean (standard error) | 22.25 (± 6.08) | -13.3 (± 6.16) | -26.6 (± 6.3) | -35.8 (± 6.29) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | -17.6 (± 6.01) | -23.6 (± 5.87) | -23.2 (± 6.18) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -35.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -51.1 |
| upper limit | -20 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.89 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -48.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -64.5 |
| upper limit | -33.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.98 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -73.7 |
| upper limit | -42.4 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.97 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -39.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -55.3 |
| upper limit | -24.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.84 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -45.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -61.2 |
| upper limit | -30.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.82 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -45.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -61.1 |
| upper limit | -29.9 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.93 |

Secondary: Percent change in LDL-C

| | |
|---------------------------------|-------------------------|
| End point title | Percent change in LDL-C |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 54 |
| Units: percent | | | | |
| least squares mean (standard error) | -3.01 (± 3.56) | 5 (± 3.61) | 13.06 (± 3.68) | 17.49 (± 3.7) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | 6.18 (± 3.52) | 8.21 (± 3.43) | 12.65 (± 3.62) | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.084 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 8.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.08 |
| upper limit | 17.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.62 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 16.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.88 |
| upper limit | 25.24 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.67 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 20.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.3 |
| upper limit | 29.68 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.67 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.046 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 9.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.15 |
| upper limit | 18.22 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.59 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.015 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 11.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.21 |
| upper limit | 20.22 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.58 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 15.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.55 |
| upper limit | 24.77 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.63 |

Secondary: Percent change in apolipoprotein A1

| | |
|---------------------------------|-------------------------------------|
| End point title | Percent change in apolipoprotein A1 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 52 |
| Units: percent | | | | |
| least squares mean (standard error) | 1.82 (± 1.9) | 6.25 (± 1.93) | 4.78 (± 1.97) | 2.23 (± 1.99) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 57 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | 1.72 (± 1.88) | 3.71 (± 1.86) | 4.47 (± 1.93) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.073 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 4.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.42 |
| upper limit | 9.28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.47 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.234 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.93 |
| upper limit | 7.86 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.49 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 108 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.871 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.53 |
| upper limit | 5.35 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.51 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.969 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.92 |
| upper limit | 4.73 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.45 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.441 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.94 |
| upper limit | 6.74 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.46 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.284 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 2.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.2 |
| upper limit | 7.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.47 |

Secondary: Percent change in apolipoprotein B

| | |
|---------------------------------|------------------------------------|
| End point title | Percent change in apolipoprotein B |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 52 |
| Units: percent | | | | |
| least squares mean (standard error) | 0.48 (± 2.94) | 2.2 (± 2.99) | -0.23 (± 3.05) | -2.71 (± 3.1) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 57 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | -1.62 (± 2.91) | -0.57 (± 2.87) | -0.89 (± 2.98) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | K-877 0.05 mg twice daily v Placebo twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.653 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.81 |
| upper limit | 9.25 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.83 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.855 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.3 |
| upper limit | 6.89 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.86 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 108 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.415 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -3.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.9 |
| upper limit | 4.5 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.91 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.582 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.57 |
| upper limit | 5.38 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.8 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.783 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.53 |
| upper limit | 6.43 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.8 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.721 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.9 |
| upper limit | 6.16 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.83 |

Secondary: Percent change in apolipoprotein C3

| | |
|---------------------------------|-------------------------------------|
| End point title | Percent change in apolipoprotein C3 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change from baseline to Week 12 | |

| End point values | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily | K-877 0.2 mg twice daily |
|-------------------------------------|---------------------|---------------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 56 | 54 | 52 |
| Units: percent | | | | |
| least squares mean (standard error) | 5.13 (± 3.85) | -10.3 (± 3.9) | -23.6 (± 3.98) | -30.8 (± 4.04) |

| End point values | K-877 0.1 mg once daily | K-877 0.2 mg once daily | K-877 0.4 mg once daily | |
|-------------------------------------|-------------------------|-------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 57 | 56 | |
| Units: percent | | | | |
| least squares mean (standard error) | -12 (± 3.82) | -19.2 (± 3.75) | -18.6 (± 3.92) | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.05 mg twice daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -15.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -25.3 |
| upper limit | -5.63 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 5 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg twice daily |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -28.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38.6 |
| upper limit | -18.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 5.05 |

| | |
|---|--|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg twice daily |
| Number of subjects included in analysis | 108 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -46 |
| upper limit | -25.9 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 5.1 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.1 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -17.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -26.9 |
| upper limit | -7.28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.99 |

| | |
|---|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.2 mg once daily |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -24.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -34.1 |
| upper limit | -14.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.97 |

| | |
|-----------------------------------|---|
| Statistical analysis title | ANCOVA Analysis |
| Comparison groups | Placebo twice daily v K-877 0.4 mg once daily |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -23.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -33.6 |
| upper limit | -13.9 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 5.01 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were to be reported from signing of the Informed Consent Form until the last study visit. Serious adverse events were to be collected from signing of the Informed Consent Form until 30 days after the last dose of study medication.

Adverse event reporting additional description:

Only treatment-emergent adverse events (i.e. events not present prior to the initiation of the study drugs or events already present that worsens in either intensity or frequency following exposure to the study drugs) are summarised here.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 16.0 |

Reporting groups

| | |
|--------------------------------|---------------------------|
| Reporting group title | Placebo twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.05 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.1 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.2 mg twice daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.1 mg once daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.2 mg once daily |
| Reporting group description: - | |
| Reporting group title | K-877 0.4 mg once daily |
| Reporting group description: - | |

| Serious adverse events | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily |
|---|---------------------|---------------------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Laryngeal polyp | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung cancer metastatic | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | K-877 0.2 mg twice daily | K-877 0.1 mg once daily | K-877 0.2 mg once daily |
|--|--------------------------|-------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 3 / 58 (5.17%) | 2 / 58 (3.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Laryngeal polyp | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 58 (1.72%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 58 (1.72%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 58 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 58 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 58 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 58 (1.72%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 58 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 58 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 58 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-------------------------|--|--|
| Serious adverse events | K-877 0.4 mg once daily | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Laryngeal polyp | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |

| | | | |
|---|----------------|--|--|
| Hypertension | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | | |
| 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 | Placebo twice daily | K-877 0.05 mg twice daily | K-877 0.1 mg twice daily |
|---|---------------------|---------------------------|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 34 / 60 (56.67%) | 29 / 57 (50.88%) | 21 / 58 (36.21%) |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences (all) | 2 | 0 | 1 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | 0 / 57 (0.00%) | 2 / 58 (3.45%) |
| occurrences (all) | 2 | 0 | 2 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 60 (8.33%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 0 / 57 (0.00%) | 3 / 58 (5.17%) |
| occurrences (all) | 1 | 0 | 3 |
| Back pain | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | 1 / 57 (1.75%) | 1 / 58 (1.72%) |
| occurrences (all) | 3 | 1 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | 1 / 57 (1.75%) | 1 / 58 (1.72%) |
| occurrences (all) | 2 | 1 | 1 |
| Influenza | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 60 (3.33%) 2 | 1 / 57 (1.75%) 1 | 3 / 58 (5.17%) 3 |
| Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all) | 3 / 60 (5.00%) 3 | 2 / 57 (3.51%) 2 | 1 / 58 (1.72%) 1 |

| Non-serious adverse events | K-877 0.2 mg twice daily | K-877 0.1 mg once daily | K-877 0.2 mg once daily |
|---|--------------------------|-------------------------|-------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 30 / 57 (52.63%) | 22 / 58 (37.93%) | 29 / 58 (50.00%) |
| Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 58 (1.72%) 1 | 4 / 58 (6.90%) 4 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 4 / 57 (7.02%) 4 | 2 / 58 (3.45%) 2 | 3 / 58 (5.17%) 3 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 3 / 57 (5.26%) 3 | 0 / 58 (0.00%) 0 | 0 / 58 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 58 (1.72%) 1 | 1 / 58 (1.72%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 4 / 58 (6.90%) 4 | 0 / 58 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 3 / 57 (5.26%) 3 | 0 / 58 (0.00%) 0 | 1 / 58 (1.72%) 1 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 5 / 57 (8.77%) 5 | 2 / 58 (3.45%) 2 | 4 / 58 (6.90%) 4 |
| Urinary tract infection | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 57 (1.75%) 1 | 2 / 58 (3.45%) 2 | 1 / 58 (1.72%) 1 |
| Influenza subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 0 / 58 (0.00%) 0 | 1 / 58 (1.72%) 1 |
| Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all) | 0 / 57 (0.00%) 0 | 1 / 58 (1.72%) 1 | 3 / 58 (5.17%) 3 |

| | | | |
|---|-------------------------|--|--|
| Non-serious adverse events | K-877 0.4 mg once daily | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 30 / 59 (50.85%) | | |
| Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | | |
| Back pain subjects affected / exposed occurrences (all) | 2 / 59 (3.39%) 2 | | |
| Muscle spasms subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | | |
| Infections and infestations | | | |

| | | | |
|---|---------------------|--|--|
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 59 (6.78%) 4 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 4 / 59 (6.78%) 4 | | |
| Influenza subjects affected / exposed occurrences (all) | 1 / 59 (1.69%) 1 | | |
| Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 17 October 2013 | The protocol was amended to modify the followings. - Diaphragm with spermicide as an effective method of contraception for male or female study participants was removed from the inclusion criteria. - The inclusion criteria was added to require male study participants to use a condom with a spermicide during sexual intercourse, from screening to the end of the study, even if their sexual partner is or may be pregnant. - Subgroup analyses and non-compartmental PK analysis methods were added to the statistical analyses. |
| 18 March 2014 | The protocol was amended to allow for the inclusion of subjects who are taking the maximum tolerated dose of statin and still have not reached the LDL-C targets as defined in the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported