# Clinical trial results:
# A multi-centre, randomised, double-blind placebo-controlled, Phase 2 study to investigate efficacy, safety and tolerability of SLN360 in participants with elevated lipoprotein(a) at high risk of atherosclerotic cardiovascular disease events

## Summary

| | |
|---|---|
| EudraCT number | 2022-001876-32 |
| Trial protocol | ES NL SK DK CZ |
| Global end of trial date | 01 July 2024 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 June 2025 |
| First version publication date | 14 June 2025 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | SLN360-002 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05537571 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Silence Therapeutics plc |
| Sponsor organisation address | 72 Hammersmith Road, London, United Kingdom, W14 8TH |
| Public contact | Global Regulatory, Silence Therapeutics plc, global-regulatory@silence-therapeutics.com |
| Scientific contact | Global Regulatory, Silence Therapeutics plc, global-regulatory@silence-therapeutics.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 16 July 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 01 July 2024 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to evaluate the effect of SLN360 on circulating levels of lipoprotein(a) in participants with elevated lipoprotein(a) at high risk of ASCVD events.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation Good Clinical Practice regulations/guidelines.

Background therapy:

Participants received standard of care stable doses of lipid-modifying therapy during the trial.

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 December 2022 |
| 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 | Netherlands: 60 |
| Country: Number of subjects enrolled | Slovakia: 5 |
| Country: Number of subjects enrolled | Czechia: 11 |
| Country: Number of subjects enrolled | Denmark: 25 |
| Country: Number of subjects enrolled | United Kingdom: 32 |
| Country: Number of subjects enrolled | Australia: 18 |
| Country: Number of subjects enrolled | South Africa: 29 |
| Worldwide total number of subjects | 180 |
| EEA total number of subjects | 101 |

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) | 92 |
| From 65 to 84 years | 88 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were screened from 05 December 2022, first randomised participant signed informed consent on 13 December 2022 and last participant was randomised 27 April 2023.

### Pre-assignment

Screening details:

A total of 253 participants were screened for inclusion, 73 participants failed screening.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 253[1] |
| Number of subjects completed | 180[2] |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Adverse event, non-fatal: 2 |
| Reason: Number of subjects | Consent withdrawn by subject: 1 |
| Reason: Number of subjects | Other: 4 |
| Reason: Number of subjects | Failure to meet randomisation criteria: 66 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number includes enrolled participants whereas the pre-assignment period includes participants who failed screening and were not enrolled.
[2] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.
Justification: The pre-assignment period represents the screening period, reasons for non-completion are provided. The 180 participants included in period 1 include those participants who did not fail screening and who were enrolled and randomised.

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

Following the completion of 36 weeks, limited members from the Sponsor team were unblinded. The nature of the treatment supply meant that the pharmacist was unblinded with appropriate unblinded oversight in place.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | Placebo Q16W |

Arm description:

Placebo administered subcutaneously at Weeks 0, 16 and 32 (dosing every 16 weeks [Q16W]).

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| **Arm title** | Placebo Q24W |
|---|---|

Arm description:

Placebo administered subcutaneously at Weeks 0 and 24 (dosing every 24 weeks [Q24W]). This group was stratified so that half of participants were dosed to match the SLN360 300 mg Q24W group and half were dosed to match the SLN360 450 mg Q24W group (with respect to injected volume).

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| **Arm title** | SLN360 300 mg Q16W |
|---|---|

Arm description:

SLN360 300 mg administered subcutaneously at Weeks 0, 16 and 32 (Q16W).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Zerlasiran |
| Investigational medicinal product code | SLN360 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| **Arm title** | SLN360 300 mg Q24W |
|---|---|

Arm description:

SLN360 300 mg administered subcutaneously at Weeks 0 and 24 (Q24W).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Zerlasiran |
| Investigational medicinal product code | SLN360 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| **Arm title** | SLN360 450 mg Q24W |
|---|---|

Arm description:

SLN360 450 mg administered subcutaneously at Weeks 0 and 24 (Q24W).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Zerlasiran |
| Investigational medicinal product code | SLN360 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| **Arm title** | Pooled placebo |
|---|---|

Arm description:

Pooled data from both placebo groups.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| **Number of subjects in period 1** | Placebo Q16W | Placebo Q24W | SLN360 300 mg Q16W |
|---|---|---|---|
| Started | 23 | 24 | 44 |
| Treated | 23 | 24 | 42 |
| Completed | 23 | 23 | 39 |
| Not completed | 0 | 1 | 5 |
| Consent withdrawn by subject | - | - | 1 |
| Adverse event, non-fatal | - | - | 2 |
| Lost to follow-up | - | 1 | - |
| Hepatitis A screening result | - | - | 2 |

| **Number of subjects in period 1** | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|
| Started | 44 | 45 | 47 |
| Treated | 44 | 45 | 47 |
| Completed | 43 | 44 | 46 |
| Not completed | 1 | 1 | 1 |
| Consent withdrawn by subject | 1 | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | 1 | 1 |
| Hepatitis A screening result | - | - | - |

| **Period 2** | |
|---|---|
| Period 2 title | Treatment and follow-up |
| Is this the baseline period? | Yes[3] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

Following the completion of 36 weeks, limited members from the Sponsor team were unblinded. The

nature of the treatment supply meant that the pharmacist was unblinded with appropriate unblinded oversight in place.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | Placebo Q16W |

Arm description:

Placebo administered subcutaneously at Weeks 0, 16 and 32 (dosing every 16 weeks [Q16W]).

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|---|---|
| **Arm title** | Placebo Q24W |

Arm description:

Placebo administered subcutaneously at Weeks 0 and 24 (dosing every 24 weeks [Q24W]). This group was stratified so that half of participants were dosed to match the SLN360 300 mg Q24W group and half were dosed to match the SLN360 450 mg Q24W group (with respect to injected volume).

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|---|---|
| **Arm title** | SLN360 300 mg Q16W |

Arm description:

SLN360 300 mg administered subcutaneously at Weeks 0, 16 and 32 (Q16W).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Zerlasiran |
| Investigational medicinal product code | SLN360 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|---|---|
| **Arm title** | SLN360 300 mg Q24W |

Arm description:

SLN360 300 mg administered subcutaneously at Weeks 0 and 24 (Q24W).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Zerlasiran |
| Investigational medicinal product code | SLN360 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered by subcutaneous injection.

| | |
|---|---|
| **Arm title** | SLN360 450 mg Q24W |

| | |
|---|---|
| Arm description: | |
| SLN360 450 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Arm type | Experimental |
| Investigational medicinal product name | Zerlasiran |
| Investigational medicinal product code | SLN360 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Administered by subcutaneous injection. | |
| **Arm title** | Pooled placebo |
| Arm description: | |
| Pooled data from both placebo groups. | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Administered by subcutaneous injection. | |

Notes:

[3] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Of the 180 enrolled and randomised participants, 2 participants randomised to the SLN360 300 mg Q16W group were untreated because both participants were determined to be ineligible before study drug could be administered due to hepatitis A screening results; both participants were terminated early from the study, rescreened and underwent a second randomisation, following which the participants were treated with SLN360 300 mg Q16W and SLN360 300 mg Q24W, respectively.

| **Number of subjects in period 2** | Placebo Q16W | Placebo Q24W | SLN360 300 mg Q16W |
|---|---|---|---|
| Started | 23 | 24 | 42 |
| Completed | 23 | 23 | 39 |
| Not completed | 0 | 1 | 3 |
| Consent withdrawn by subject | - | - | 1 |
| Adverse event, non-fatal | - | - | 2 |
| Lost to follow-up | - | 1 | - |

| **Number of subjects in period 2** | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|
| Started | 44 | 45 | 47 |
| Completed | 43 | 44 | 46 |
| Not completed | 1 | 1 | 1 |
| Consent withdrawn by subject | 1 | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | 1 | 1 |

## Baseline characteristics

| Reporting groups[1] | |
|---|---|
| Reporting group title | Placebo Q16W |
| Reporting group description: | |
| Placebo administered subcutaneously at Weeks 0, 16 and 32 (dosing every 16 weeks [Q16W]). | |
| Reporting group title | Placebo Q24W |
| Reporting group description: | |
| Placebo administered subcutaneously at Weeks 0 and 24 (dosing every 24 weeks [Q24W]). This group was stratified so that half of participants were dosed to match the SLN360 300 mg Q24W group and half were dosed to match the SLN360 450 mg Q24W group (with respect to injected volume). | |
| Reporting group title | SLN360 300 mg Q16W |
| Reporting group description: | |
| SLN360 300 mg administered subcutaneously at Weeks 0, 16 and 32 (Q16W). | |
| Reporting group title | SLN360 300 mg Q24W |
| Reporting group description: | |
| SLN360 300 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Reporting group title | SLN360 450 mg Q24W |
| Reporting group description: | |
| SLN360 450 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Reporting group title | Pooled placebo |
| Reporting group description: | |
| Pooled data from both placebo groups. | |

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: The baseline data are based on the set of unique participants who were randomised and treated, this excludes 2 participant numbers that enrolled but were not treated, but were later rescreened and re-randomised / treated. The worldwide number of participants is based on all allocated participant numbers enrolled rather than unique participants.

| Reporting group values | Placebo Q16W | Placebo Q24W | SLN360 300 mg Q16W |
|---|---|---|---|
| Number of subjects | 23 | 24 | 42 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 12 | 15 | 19 |
| From 65-84 years | 11 | 9 | 23 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 65.0 | 62.1 | 63.1 |
| standard deviation | ± 8.79 | ± 9.43 | ± 9.81 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 5 | 6 | 11 |
| Male | 18 | 18 | 31 |
| Ethnicity<br>Units: Subjects | | | |
| Not Hispanic or Latino | 23 | 24 | 42 |
| Race<br>Units: Subjects | | | |
| Asian | 0 | 1 | 1 |
| Black or African American | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| White | 21 | 22 | 38 |
| Other | 2 | 1 | 2 |

| **Reporting group values** | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|
| Number of subjects | 44 | 45 | 47 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 23 | 22 | 27 |
| From 65-84 years | 21 | 23 | 20 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 64.5 | 63.8 | 63.6 |
| standard deviation | ± 8.67 | ± 10.23 | ± 9.14 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 13 | 11 | 11 |
| Male | 31 | 34 | 36 |
| Ethnicity<br>Units: Subjects | | | |
| Not Hispanic or Latino | 44 | 45 | 47 |
| Race<br>Units: Subjects | | | |
| Asian | 2 | 4 | 1 |
| Black or African American | 0 | 2 | 0 |
| White | 36 | 36 | 43 |
| Other | 6 | 3 | 3 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 178 | | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 91 | | |
| From 65-84 years | 87 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 46 | | |
| Male | 132 | | |
| Ethnicity<br>Units: Subjects | | | |
| Not Hispanic or Latino | 178 | | |
| Race<br>Units: Subjects | | | |
| Asian | 8 | | |
| Black or African American | 3 | | |
| White | 153 | | |
| Other | 14 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo Q16W |
| Reporting group description: | |
| Placebo administered subcutaneously at Weeks 0, 16 and 32 (dosing every 16 weeks [Q16W]). | |
| Reporting group title | Placebo Q24W |
| Reporting group description: | |
| Placebo administered subcutaneously at Weeks 0 and 24 (dosing every 24 weeks [Q24W]). This group was stratified so that half of participants were dosed to match the SLN360 300 mg Q24W group and half were dosed to match the SLN360 450 mg Q24W group (with respect to injected volume). | |
| Reporting group title | SLN360 300 mg Q16W |
| Reporting group description: | |
| SLN360 300 mg administered subcutaneously at Weeks 0, 16 and 32 (Q16W). | |
| Reporting group title | SLN360 300 mg Q24W |
| Reporting group description: | |
| SLN360 300 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Reporting group title | SLN360 450 mg Q24W |
| Reporting group description: | |
| SLN360 450 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Reporting group title | Pooled placebo |
| Reporting group description: | |
| Pooled data from both placebo groups. | |
| Reporting group title | Placebo Q16W |
| Reporting group description: | |
| Placebo administered subcutaneously at Weeks 0, 16 and 32 (dosing every 16 weeks [Q16W]). | |
| Reporting group title | Placebo Q24W |
| Reporting group description: | |
| Placebo administered subcutaneously at Weeks 0 and 24 (dosing every 24 weeks [Q24W]). This group was stratified so that half of participants were dosed to match the SLN360 300 mg Q24W group and half were dosed to match the SLN360 450 mg Q24W group (with respect to injected volume). | |
| Reporting group title | SLN360 300 mg Q16W |
| Reporting group description: | |
| SLN360 300 mg administered subcutaneously at Weeks 0, 16 and 32 (Q16W). | |
| Reporting group title | SLN360 300 mg Q24W |
| Reporting group description: | |
| SLN360 300 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Reporting group title | SLN360 450 mg Q24W |
| Reporting group description: | |
| SLN360 450 mg administered subcutaneously at Weeks 0 and 24 (Q24W). | |
| Reporting group title | Pooled placebo |
| Reporting group description: | |
| Pooled data from both placebo groups. | |

### Primary: Time-averaged percent change in lipoprotein(a) molar concentration from baseline to Week 36

| | |
|---|---|
| End point title | Time-averaged percent change in lipoprotein(a) molar concentration from baseline to Week 36 |

End point description:

In calculating the primary outcome measure, the time-averaged percent change in lipoprotein(a)

(relative to Day 1 predose) was calculated for each participant by estimating the sum of the area under the curve with the linear trapezoidal method for all scheduled assessments from Week 4 to Week 36, inclusive, divided by the total time interval between the Week 4 and Week 36 assessments. Analysis of variance was used to test for differences between each active treatment group and the pooled placebo groups in the primary outcome measure. Time-averaged percent change in lipoprotein(a) to Week 36 was the dependent variable, and treatment group was included as the predictor variable. The least squares (LS) means, standard errors, and 2-sided 95% confidence intervals (CIs) for each treatment group and for the pairwise comparisons between the SLN360 and placebo groups were estimated.

| End point type | Primary |
|---|---|
| End point timeframe: | |
| Week 36 relative to baseline | |

| **End point values** | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -80.5 (± 1.99) | -79.1 (± 1.94) | -83.3 (± 1.92) | 2.3 (± 1.88) |

**Statistical analyses**

| **Statistical analysis title** | Analysis of variance for the primary endpoint |
|---|---|
| Statistical analysis description: | |
| Analysis of variance (ANOVA) was used to test for differences between each active treatment group and the pooled placebo groups in the primary outcome measure. | |
| Comparison groups | Pooled placebo v SLN360 300 mg Q16W |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -82.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -88.19 |
| upper limit | -77.39 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the primary endpoint |
|---|---|
| Statistical analysis description: | |
| Analysis of variance (ANOVA) was used to test for differences between each active treatment group and the pooled placebo groups in the primary outcome measure. | |
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |

| | |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -81.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -86.68 |
| upper limit | -76 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the primary endpoint |
|---|---|
| Statistical analysis description: | |
| Analysis of variance (ANOVA) was used to test for differences between each active treatment group and the pooled placebo groups in the primary outcome measure. | |
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -85.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -90.88 |
| upper limit | -80.26 |

## Secondary: Time-averaged percent change in lipoprotein(a) molar concentration from baseline to Week 48

| End point title | Time-averaged percent change in lipoprotein(a) molar concentration from baseline to Week 48 |
|---|---|
| End point description: | |
| Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 48 relative to baseline | |

| End point values | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -81.6 (± 2.05) | -77.2 (± 2.00) | -81.5 (± 1.98) | 1.5 (± 1.94) |

**Statistical analyses**

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -83.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -88.7 |
| upper limit | -77.57 |
| Variability estimate | Standard error of the mean |

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | Pooled placebo v SLN360 300 mg Q24W |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -78.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -84.18 |
| upper limit | -73.17 |
| Variability estimate | Standard error of the mean |

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | Pooled placebo v SLN360 450 mg Q24W |

| | |
|---|---|
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -88.43 |
| upper limit | -77.49 |
| Variability estimate | Standard error of the mean |

## Secondary: Time-averaged percent change in lipoprotein(a) molar concentration from baseline to Week 60

| | |
|---|---|
| End point title | Time-averaged percent change in lipoprotein(a) molar concentration from baseline to Week 60 |

End point description:

Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint.

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

End point timeframe:

Week 60 relative to baseline

| End point values | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -78.0 (± 2.24) | -70.7 (± 2.19) | -76.0 (± 2.16) | 1.1 (± 2.11) |

### Statistical analyses

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -79.2 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -85.25 |
| upper limit | -73.1 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -71.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -77.81 |
| upper limit | -65.8 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -77.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -83.09 |
| upper limit | -71.15 |
| Variability estimate | Standard error of the mean |

## Secondary: Time-averaged percent change in apolipoprotein(B) concentration from baseline to Week 36

| | |
|---|---|
| End point title | Time-averaged percent change in apolipoprotein(B) concentration from baseline to Week 36 |

| | |
|---|---|
| End point description: | |
| Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 36 relative to baseline | |

| **End point values** | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -16.9 (± 1.93) | -13.5 (± 1.88) | -18.6 (± 1.86) | -3.6 (± 1.82) |

**Statistical analyses**

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | Pooled placebo v SLN360 300 mg Q16W |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -13.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.55 |
| upper limit | -8.09 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0002 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -9.9 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.02 |
| upper limit | -4.68 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.1 |
| upper limit | -9.82 |
| Variability estimate | Standard error of the mean |

**Secondary: Time-averaged percent change in apolipoprotein(B) concentration from baseline to Week 48**

| End point title | Time-averaged percent change in apolipoprotein(B) concentration from baseline to Week 48 |
|---|---|

End point description:

Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint.

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

End point timeframe:

Week 48 relative to baseline

| **End point values** | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -16.4 (± 1.94) | -12.6 (± 1.90) | -18.0 (± 1.88) | -4.0 (± 1.83) |

**Statistical analyses**

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -12.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.62 |
| upper limit | -7.08 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0013 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -8.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.85 |
| upper limit | -3.44 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.2 |
| upper limit | -8.84 |

| | |
|---|---|
| Variability estimate | Standard error of the mean |

## Secondary: Time-averaged percent change in apolipoprotein(B) concentration from baseline to Week 60

| | |
|---|---|
| End point title | Time-averaged percent change in apolipoprotein(B) concentration from baseline to Week 60 |

End point description:

Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint.

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

End point timeframe:

Week 60 relative to baseline

| End point values | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -15.0 (± 2.04) | -10.9 (± 1.99) | -16.4 (± 1.97) | -3.8 (± 1.93) |

### Statistical analyses

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -11.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.81 |
| upper limit | -5.73 |
| Variability estimate | Standard error of the mean |

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |

| | |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0106 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -7.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.64 |
| upper limit | -1.69 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -12.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.04 |
| upper limit | -7.15 |
| Variability estimate | Standard error of the mean |

## Secondary: Time-averaged percent change in low-density lipoprotein cholesterol concentration from baseline to Week 36

| End point title | Time-averaged percent change in low-density lipoprotein cholesterol concentration from baseline to Week 36 |
|---|---|

End point description:

Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint.

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

End point timeframe:

Week 36 relative to baseline

| End point values | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -22.3 (± 8.16) | -20.1 (± 7.98) | -15.5 (± 7.89) | 9.6 (± 7.72) |

**Statistical analyses**

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0051 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -31.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -54.07 |
| upper limit | -9.72 |
| Variability estimate | Standard error of the mean |

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0081 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -29.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -51.62 |
| upper limit | -7.81 |
| Variability estimate | Standard error of the mean |

| Statistical analysis title | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | Pooled placebo v SLN360 450 mg Q24W |

| | |
|---|---|
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0241 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -25.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -46.89 |
| upper limit | -3.33 |
| Variability estimate | Standard error of the mean |

## Secondary: Time-averaged percent change in low-density lipoprotein cholesterol concentration from baseline to Week 48

| | |
|---|---|
| End point title | Time-averaged percent change in low-density lipoprotein cholesterol concentration from baseline to Week 48 |

End point description:

Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint.

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

End point timeframe:

Week 48 relative to baseline

| **End point values** | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -20.9 (± 7.01) | -18.5 (± 6.85) | -17.0 (± 6.78) | 8.9 (± 6.63) |

### Statistical analyses

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0023 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -29.8 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -48.86 |
| upper limit | -10.76 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0046 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -27.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -46.23 |
| upper limit | -8.58 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0068 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -44.67 |
| upper limit | -7.24 |
| Variability estimate | Standard error of the mean |

## Secondary: Time-averaged percent change in low-density lipoprotein cholesterol concentration from baseline to Week 60

| | |
|---|---|
| End point title | Time-averaged percent change in low-density lipoprotein cholesterol concentration from baseline to Week 60 |

End point description:

Time-averaged secondary endpoints were calculated and analysed using the same conventions as the primary endpoint.

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

End point timeframe:

Week 60 relative to baseline

| **End point values** | SLN360 300 mg Q16W | SLN360 300 mg Q24W | SLN360 450 mg Q24W | Pooled placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 42 | 44 | 45 | 47 |
| Units: Percentage | | | | |
| least squares mean (standard error) | -19.3 (± 7.45) | -16.8 (± 7.28) | -14.7 (± 7.19) | 9.3 (± 7.04) |

**Statistical analyses**

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q16W v Pooled placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0057 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -28.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -48.91 |
| upper limit | -8.46 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 300 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0106 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -26.1 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -46.13 |
| upper limit | -6.16 |
| Variability estimate | Standard error of the mean |

| **Statistical analysis title** | Analysis of variance for the secondary endpoint |
|---|---|
| Comparison groups | SLN360 450 mg Q24W v Pooled placebo |
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0179 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -24.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -43.93 |
| upper limit | -4.2 |
| Variability estimate | Standard error of the mean |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

05 December 2022 (first participant screened) to 01 July 2024 (last participant last visit). Median duration of exposure was 24.43 weeks. Adverse event data were collected over the 60-week study period (95.6% of participants completed to week 60).

Adverse event reporting additional description:

Serious treatment-emergent and non-serious treatment-emergent adverse events are summarised for the safety population: all participants who received at least 1 dose of study drug. Safety data were summarised by actual treatment received based on the safety population.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo Q16W |

Reporting group description:

Placebo administered subcutaneously at Weeks 0, 16 and 32 (dosing every 16 weeks [Q16W]).

| | |
|---|---|
| Reporting group title | Placebo Q24W |

Reporting group description:

Placebo administered subcutaneously at Weeks 0 and 24 (dosing every 24 weeks [Q24W]). This group was stratified so that half of participants were dosed to match the SLN360 300 mg Q24W group and half were dosed to match the SLN360 450 mg Q24W group (with respect to injected volume).

| | |
|---|---|
| Reporting group title | SLN360 300 mg Q16W |

Reporting group description:

SLN360 300 mg administered subcutaneously at Weeks 0, 16 and 32 (Q16W).

| | |
|---|---|
| Reporting group title | SLN360 300 mg Q24W |

Reporting group description:

SLN360 300 mg administered subcutaneously at Weeks 0 and 24 (Q24W).

| | |
|---|---|
| Reporting group title | SLN360 450 mg Q24W |

Reporting group description:

SLN360 450 mg administered subcutaneously at Weeks 0 and 24 (Q24W).

| Serious adverse events | Placebo Q16W | Placebo Q24W | SLN360 300 mg Q16W |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 3 / 24 (12.50%) | 6 / 42 (14.29%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant polyp (rectal) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 0 / 42 (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 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 0 / 42 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 24 (0.00%) | 0 / 42 (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 |
| Nervous system disorders | | | |
| Acute vestibular syndrome | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 24 (4.17%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Food poisoning | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| 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 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polymyositis | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| 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 | | | |
| Lymph node tuberculosis | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 0 / 42 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 24 (4.17%) | 0 / 42 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 24 (4.17%) | 0 / 42 (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 |

| **Serious adverse events** | SLN360 300 mg Q24W | SLN360 450 mg Q24W | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 44 (4.55%) | 5 / 45 (11.11%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant polyp (rectal) | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 44 (2.27%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Acute vestibular syndrome | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Musculoskeletal and connective tissue disorders** | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polymyositis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Infections and infestations** | | | |
| Lymph node tuberculosis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo Q16W | Placebo Q24W | SLN360 300 mg Q16W |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 23 (78.26%) | 22 / 24 (91.67%) | 42 / 42 (100.00%) |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 24 (0.00%) | 4 / 42 (9.52%) |
| occurrences (all) | 2 | 0 | 8 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 24 (0.00%) | 0 / 42 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 3 / 24 (12.50%) | 1 / 42 (2.38%) |
| occurrences (all) | 2 | 3 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 24 (4.17%) | 3 / 42 (7.14%) |
| occurrences (all) | 1 | 1 | 3 |
| Headache | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 24 (4.17%) | 5 / 42 (11.90%) |
| occurrences (all) | 1 | 1 | 5 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 1 / 24 (4.17%) | 0 / 42 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Influenza-like illness | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 24 (4.17%) | 2 / 42 (4.76%) |
| occurrences (all) | 0 | 1 | 2 |
| Injection site reaction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 23 (8.70%) | 2 / 24 (8.33%) | 35 / 42 (83.33%) |
| occurrences (all) | 3 | 2 | 71 |
| Malaise | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 24 (4.17%) | 6 / 42 (14.29%) |
| occurrences (all) | 0 | 1 | 8 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 1 / 24 (4.17%) | 0 / 42 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 2 / 24 (8.33%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 2 / 24 (8.33%) | 1 / 42 (2.38%) |
| occurrences (all) | 1 | 2 | 2 |
| Haemorrhoids | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 24 (0.00%) | 0 / 42 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 2 / 24 (8.33%) | 1 / 42 (2.38%) |
| occurrences (all) | 2 | 2 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 2 / 24 (8.33%) | 0 / 42 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 24 (0.00%) | 3 / 42 (7.14%) |
| occurrences (all) | 2 | 0 | 4 |
| Back pain | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 24 (0.00%) | 2 / 42 (4.76%) |
| occurrences (all) | 2 | 0 | 2 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 24 (4.17%) | 1 / 42 (2.38%) |
| occurrences (all) | 1 | 1 | 2 |
| Osteoarthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 23 (0.00%) | 2 / 24 (8.33%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 2 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 0 / 24 (0.00%) | 2 / 42 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 4 / 24 (16.67%) | 2 / 42 (4.76%) |
| occurrences (all) | 3 | 4 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 24 (0.00%) | 3 / 42 (7.14%) |
| occurrences (all) | 2 | 0 | 3 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 23 (8.70%) | 0 / 24 (0.00%) | 0 / 42 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 3 / 24 (12.50%) | 6 / 42 (14.29%) |
| occurrences (all) | 1 | 6 | 7 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 0 / 24 (0.00%) | 5 / 42 (11.90%) |
| occurrences (all) | 4 | 0 | 6 |

| **Non-serious adverse events** | SLN360 300 mg Q24W | SLN360 450 mg Q24W | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 43 / 44 (97.73%) | 42 / 45 (93.33%) | |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 2 / 45 (4.44%) | |
| occurrences (all) | 1 | 4 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 2 / 45 (4.44%) | |
| occurrences (all) | 1 | 2 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 44 (2.27%) | 2 / 45 (4.44%) | |
| occurrences (all) | 2 | 2 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 44 (9.09%) | 1 / 45 (2.22%) | |
| occurrences (all) | 5 | 1 | |
| Headache | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 6 / 45 (13.33%) | |
| occurrences (all) | 5 | 8 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 44 (9.09%) | 1 / 45 (2.22%) | |
| occurrences (all) | 4 | 1 | |
| Influenza-like illness | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 7 / 45 (15.56%) | |
| occurrences (all) | 1 | 7 | |
| Injection site reaction | | | |
| subjects affected / exposed | 36 / 44 (81.82%) | 37 / 45 (82.22%) | |
| occurrences (all) | 55 | 109 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 4 / 45 (8.89%) | |
| occurrences (all) | 0 | 5 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 0 / 45 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 2 / 45 (4.44%) | |
| occurrences (all) | 0 | 2 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 1 / 45 (2.22%) | |
| occurrences (all) | 1 | 1 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 44 (2.27%) | 1 / 45 (2.22%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 44 (4.55%) | 0 / 45 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 4 / 44 (9.09%) | 2 / 45 (4.44%) | |
| occurrences (all) | 4 | 2 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 44 (4.55%) | 0 / 45 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 7 / 45 (15.56%) | |
| occurrences (all) | 1 | 8 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 45 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 3 / 45 (6.67%) | |
| occurrences (all) | 1 | 3 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 6 / 44 (13.64%) | 4 / 45 (8.89%) | |
| occurrences (all) | 7 | 4 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 44 (13.64%) | 6 / 45 (13.33%) | |
| occurrences (all) | 8 | 9 | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | 1 / 45 (2.22%) | |
| occurrences (all) | 0 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 44 (15.91%) | 5 / 45 (11.11%) | |
| occurrences (all) | 8 | 5 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 44 (2.27%)<br>2 | 3 / 45 (6.67%)<br>4 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/39556769