



## Clinical trial results:

**Dose response and safety of an oral PCSK9i, NNC0385-0434, in patients with established atherosclerotic cardiovascular disease (ASCVD) or ASCVD risk on maximally tolerated statin dose and other lipid-lowering therapy requiring further LDL-C reduction**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-002630-32 |
| Trial protocol           | DE GR NL BE PL |
| Global end of trial date | 20 June 2022   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 04 July 2023 |
| First version publication date | 04 July 2023 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | NN6435-4697 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT04992065     |
| WHO universal trial number (UTN)   | U1111-1252-3392 |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Novo Nordisk A/S   |
| Sponsor organisation address | Novo Allé, Bagsvaerd, Denmark, 2880  |
| Public contact               | Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact           | Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.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                       | 27 July 2022 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 20 June 2022 |
| Was the trial ended prematurely? | No           |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate superiority of three dose levels of oral NNC0385-0434 versus placebo on percent change in low-density lipoprotein cholesterol (LDL-C) from baseline to week 12 in subjects with established ASCVD or ASCVD risk on maximally tolerated statin dose and other lipid-lowering therapy requiring further LDL-C reduction.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki and International Council of Harmonisation (ICH) Good Clinical Practice, including archiving of essential documents and Food and Drug Administration (FDA) 21 Code of Federal Regulation (CFR) 312.120.

Background therapy:

Subjects were to continue their background medication (maximally tolerated dose of statins and other lipid-lowering therapies [except proprotein convertase subtilisin/kexin type 9 inhibition {PCSK9i} therapy, PCSK9 small interfering ribonucleic acid {siRNA} therapy and oral semaglutide therapy]) throughout the entire trial.

Evidence for comparator:

Not applicable.

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 03 August 2021 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | Yes            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Belgium: 21       |
| Country: Number of subjects enrolled | Germany: 38       |
| Country: Number of subjects enrolled | Greece: 31        |
| Country: Number of subjects enrolled | Japan: 29         |
| Country: Number of subjects enrolled | Netherlands: 47   |
| Country: Number of subjects enrolled | Poland: 44        |
| Country: Number of subjects enrolled | United States: 57 |
| Worldwide total number of subjects   | 267               |
| EEA total number of subjects         | 181               |

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)                      | 128 |
| From 65 to 84 years                       | 139 |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at 42 sites in 7 countries as follows (number of sites that screened subjects/ number of sites that randomised subjects): Belgium (5/ 5); Germany (4/ 4); Greece (6/ 6); Japan (4/ 4); Netherlands (6/ 6); Poland (5/ 5); United States (12/ 12).

### Pre-assignment

Screening details:

Subjects were randomized to receive either one of 3 dose levels of NNC0385-0434, placebo (matched to NNC0385-0434) or evolocumab for 12 weeks.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator          |

Blinding implementation details:

The trial was double-blinded within dose level of oral NNC0385-0434 and size matched placebo arm. The subcutaneous (s.c.) evolocumab arm was open label.

### Arms

|                              |                    |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes                |
| <b>Arm title</b>             | NNC0385-0434 15 mg |

Arm description:

Subjects received 15 milligrams (mg) NNC0385-0434 (co-formulated with 500 mg salcaprozate sodium [SNAC]) tablet orally once daily for 12 weeks.

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | NNC0385-0434 A 15 mg |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Tablet               |
| Routes of administration               | Oral use             |

Dosage and administration details:

Subjects received 15 mg NNC0385-0434 once daily in the morning in a fasting state. Subjects were advised to take tablet at least 30 minutes (min) before the first food, beverage or other oral medications of the day with up to half a glass of water (approximately 120 milliliters [mL]/ 4 fluid ounces).

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | NNC0385-0434 40 mg |
|------------------|--------------------|

Arm description:

Subjects received 40 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | NNC0385-0434 A 40 mg |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Tablet               |
| Routes of administration               | Oral use             |

Dosage and administration details:

Subjects received 40 mg NNC0385-0434 once daily in the morning in a fasting state. Subjects were advised to take tablet at least 30 min before the first food, beverage or other oral medications of the day with up to half a glass of water (approximately 120 mL/ 4 fluid ounces).

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | NNC0385-0434 100 mg |
|------------------|---------------------|

**Arm description:**

Subjects received 100 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | NNC0385-0434 A 100 mg |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Tablet                |
| Routes of administration               | Oral use              |

**Dosage and administration details:**

Subjects received 100 mg NNC0385-0434 once daily in the morning in a fasting state. Subjects were advised to take tablet at least 30 min before the first food, beverage or other oral medications of the day with up to half a glass of water (approximately 120 mL/ 4 fluid ounces).

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

**Arm description:**

Subjects received placebo matched to NNC0385-0434 (without SNAC) tablet orally once daily for 12 weeks.

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Placebo                           |
| Investigational medicinal product name | Placebo (matched to NNC0385-0434) |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Tablet                            |
| Routes of administration               | Oral use                          |

**Dosage and administration details:**

Subjects received placebo matched to NNC0385-0434 once daily in the morning in a fasting state. Subjects were advised to take tablet at least 30 min before the first food, beverage or other oral medications of the day with up to half a glass of water (approximately 120 mL/ 4 fluid ounces).

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Evolocumab 140 mg |
|------------------|-------------------|

**Arm description:**

Subjects received 140 mg evolocumab injection s.c. once every weeks for 12 weeks.

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

**Dosage and administration details:**

Subjects received 140 mg evolocumab injection once every 2 weeks into areas of the abdomen, thigh, or upper arm that are not tender, bruised, red, or indurated. The evolocumab was injected using a pre-filled SureClick® autoinjector (single-use).

| <b>Number of subjects in period 1</b> | NNC0385-0434 15 mg | NNC0385-0434 40 mg | NNC0385-0434 100 mg |
|---------------------------------------|--------------------|--------------------|---------------------|
| Started                               | 53                 | 53                 | 53                  |
| Completed                             | 53                 | 53                 | 53                  |

| <b>Number of subjects in period 1</b> | Placebo | Evolocumab 140 mg |
|---------------------------------------|---------|-------------------|
| Started                               | 54      | 54                |

|           |    |    |
|-----------|----|----|
| Completed | 54 | 54 |
|-----------|----|----|

## Baseline characteristics

### Reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | NNC0385-0434 15 mg  |
| Reporting group description:<br>Subjects received 15 milligrams (mg) NNC0385-0434 (co-formulated with 500 mg salcaprozate sodium [SNAC]) tablet orally once daily for 12 weeks. |                     |
| Reporting group title   | NNC0385-0434 40 mg  |
| Reporting group description:<br>Subjects received 40 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.                                    |                     |
| Reporting group title   | NNC0385-0434 100 mg |
| Reporting group description:<br>Subjects received 100 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.                                   |                     |
| Reporting group title   | Placebo             |
| Reporting group description:<br>Subjects received placebo matched to NNC0385-0434 (without SNAC) tablet orally once daily for 12 weeks.   |                     |
| Reporting group title   | Evolocumab 140 mg   |
| Reporting group description:<br>Subjects received 140 mg evolocumab injection s.c. once every weeks for 12 weeks.   |                     |

| Reporting group values             | NNC0385-0434 15 mg | NNC0385-0434 40 mg | NNC0385-0434 100 mg |
|------------------------------------|--------------------|--------------------|---------------------|
| Number of subjects                 | 53                 | 53                 | 53                  |
| Age Categorical<br>Units: Subjects |                    |                    |                     |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 64.1<br>± 9.3 | 64.6<br>± 8.6 | 65.2<br>± 9.2 |
| Gender Categorical<br>Units: Subjects                                   |               |               |               |
| Female  | 17            | 17            | 14            |
| Male  | 36            | 36            | 39            |

| Reporting group values             | Placebo | Evolocumab 140 mg | Total |
|------------------------------------|---------|-------------------|-------|
| Number of subjects                 | 54      | 54                | 267   |
| Age Categorical<br>Units: Subjects |         |                   |       |

|   |               |               |    |
|---|---------------|---------------|----|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 63.1<br>± 8.6 | 64.5<br>± 9.6 | -  |
| Gender Categorical<br>Units: Subjects                                   |               |               |    |
| Female  | 17            | 17            | 82 |

|      |    |    |     |
|------|----|----|-----|
| Male | 37 | 37 | 185 |
|------|----|----|-----|

---

## End points

### End points reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | NNC0385-0434 15 mg  |
| Reporting group description:<br>Subjects received 15 milligrams (mg) NNC0385-0434 (co-formulated with 500 mg salcaprozate sodium [SNAC]) tablet orally once daily for 12 weeks. |                     |
| Reporting group title   | NNC0385-0434 40 mg  |
| Reporting group description:<br>Subjects received 40 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.                                    |                     |
| Reporting group title   | NNC0385-0434 100 mg |
| Reporting group description:<br>Subjects received 100 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.                                   |                     |
| Reporting group title   | Placebo             |
| Reporting group description:<br>Subjects received placebo matched to NNC0385-0434 (without SNAC) tablet orally once daily for 12 weeks.   |                     |
| Reporting group title   | Evolocumab 140 mg   |
| Reporting group description:<br>Subjects received 140 mg evolocumab injection s.c. once every weeks for 12 weeks.   |                     |

### Primary: Change in low-density lipoprotein (LDL)-cholesterol

|   |   |
|---|---|
| End point title   | Change in low-density lipoprotein (LDL)-cholesterol |
| End point description:<br>Percentage change in LDL-cholesterol (LDL-C) (measured in milligrams per deciliter [mg/dL]) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. The in-trial period is defined as the uninterrupted time interval from date of randomisation to date of last contact with trial site. Full analysis set (FAS) included all randomized subjects. Number of subjects analyzed = subjects with available data for this endpoint. |   |
| End point type  | Primary   |
| End point timeframe:<br>From baseline (week 0) to visit 9 (week 12)   |   |

| End point values                            | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|---|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                          | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed                 | 51                    | 52                    | 49                     | 52              |
| Units: Percentage change of LDL-cholesterol |                       |                       |                        |                 |
| arithmetic mean (standard deviation)        | -27 (± 19)            | -41 (± 37)            | -55 (± 20)             | 6 (± 41)        |

|   |                      |  |  |  |
|---|----------------------|--|--|--|
| <b>End point values</b>                     | Evolocumab<br>140 mg |  |  |  |
| Subject group type                          | Reporting group      |  |  |  |
| Number of subjects analysed                 | 49                   |  |  |  |
| Units: Percentage change of LDL-cholesterol |                      |  |  |  |
| arithmetic mean (standard deviation)        | -59 (± 22)           |  |  |  |

## Statistical analyses

|   |                               |
|---|-------------------------------|
| Statistical analysis title  | NNC0385-0434 15 mg vs Placebo |
| Statistical analysis description:   |                               |
| LDL-C percentage change at week 12 from baseline responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline LDL-C as covariate. |                               |
| Comparison groups   | NNC0385-0434 15 mg v Placebo  |
| Number of subjects included in analysis   | 103                           |
| Analysis specification  | Pre-specified                 |
| Analysis type   | superiority                   |
| P-value   | < 0.0001                      |
| Method  | ANCOVA                        |
| Parameter estimate  | Treatment Difference          |
| Point estimate  | -31.95                        |
| Confidence interval   |                               |
| level   | 95 %                          |
| sides   | 2-sided                       |
| lower limit   | -43.02                        |
| upper limit   | -20.87                        |

|   |                               |
|---|-------------------------------|
| Statistical analysis title  | NNC0385-0434 40 mg vs Placebo |
| Statistical analysis description:   |                               |
| LDL-C percentage change at week 12 from baseline responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline LDL-C as covariate. |                               |
| Comparison groups   | NNC0385-0434 40 mg v Placebo  |
| Number of subjects included in analysis   | 104                           |
| Analysis specification  | Pre-specified                 |
| Analysis type   | superiority                   |
| P-value   | < 0.0001                      |
| Method  | ANCOVA                        |
| Parameter estimate  | Treatment Difference          |
| Point estimate  | -44.91                        |
| Confidence interval   |                               |
| level   | 95 %                          |
| sides   | 2-sided                       |
| lower limit   | -56.04                        |
| upper limit   | -33.79                        |

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | NNC0385-0434 100 mg vs Evolocumab 140 mg |
| Statistical analysis description:   |  |
| LDL-C percentage change at week 12 from baseline responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline LDL-C as covariate. |  |
| Comparison groups   | NNC0385-0434 100 mg v Evolocumab 140 mg  |
| Number of subjects included in analysis   | 98                                       |
| Analysis specification  | Pre-specified                            |
| Analysis type   | superiority                              |
| Parameter estimate  | Treatment Difference                     |
| Point estimate  | 3.43                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | -7.81                                    |
| upper limit   | 14.68                                    |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | NNC0385-0434 15 mg vs Evolocumab 140 mg |
| Statistical analysis description:   |   |
| LDL-C percentage change at week 12 from baseline responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline LDL-C as covariate. |   |
| Comparison groups   | NNC0385-0434 15 mg v Evolocumab 140 mg  |
| Number of subjects included in analysis   | 100                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| Parameter estimate  | Treatment Difference                    |
| Point estimate  | 33.32                                   |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | 22.16                                   |
| upper limit   | 44.47                                   |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | NNC0385-0434 40 mg vs Evolocumab 140 mg |
| Statistical analysis description:   |   |
| LDL-C percentage change at week 12 from baseline responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline LDL-C as covariate. |   |
| Comparison groups   | NNC0385-0434 40 mg v Evolocumab 140 mg  |
| Number of subjects included in analysis   | 101                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| Parameter estimate  | Treatment Difference                    |
| Point estimate  | 20.35                                   |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | 9.21                                    |
| upper limit   | 31.48                                   |

|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>   | NNC0385-0434 100 mg vs Placebo |
| Statistical analysis description:   |                                |
| LDL-C percentage change at week 12 from baseline responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline LDL-C as covariate. |                                |
| Comparison groups   | NNC0385-0434 100 mg v Placebo  |
| Number of subjects included in analysis   | 101                            |
| Analysis specification  | Pre-specified                  |
| Analysis type   | superiority                    |
| P-value   | < 0.0001                       |
| Method  | ANCOVA                         |
| Parameter estimate  | Treatment Difference           |
| Point estimate  | -61.83                         |
| Confidence interval   |                                |
| level   | 95 %                           |
| sides   | 2-sided                        |
| lower limit   | -72.94                         |
| upper limit   | -50.72                         |

## Secondary: Change in total cholesterol

|  |                             |
|--|-----------------------------|
| End point title  | Change in total cholesterol |
| End point description:   |                             |
| Percentage change in total cholesterol (measured in millimoles per liter [mmol/L]) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Number of subjects analyzed = subjects with available data for this endpoint. |                             |
| End point type   | Secondary                   |
| End point timeframe:   |                             |
| From baseline (week 0) to visit 9 (week 12)  |                             |

| End point values                              | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|---|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                            | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed                   | 52                    | 52                    | 50                     | 53              |
| Units: Percentage change of total cholesterol |                       |                       |                        |                 |
| arithmetic mean (standard deviation)          | -14 (± 13)            | -25 (± 27)            | -33 (± 11)             | 4 (± 23)        |

|                         |                      |  |  |  |
|-------------------------|----------------------|--|--|--|
| <b>End point values</b> | Evolocumab<br>140 mg |  |  |  |
|-------------------------|----------------------|--|--|--|

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                            | Reporting group |  |  |  |
| Number of subjects analysed                   | 52              |  |  |  |
| Units: Percentage change of total cholesterol |                 |  |  |  |
| arithmetic mean (standard deviation)          | -38 (± 14)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in high-density lipoprotein (HDL)-cholesterol

|                 |  |
|-----------------|--|
| End point title | Change in high-density lipoprotein (HDL)-cholesterol |
|-----------------|--|

End point description:

Percentage change in HDL-cholesterol (measured in mg/dL) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Number of subjects analyzed = subjects with available data for this endpoint.

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

End point timeframe:

From baseline (week 0) to visit 9 (week 12)

| End point values                            | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|---|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                          | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed                 | 52                    | 52                    | 47                     | 53              |
| Units: Percentage change of HDL-cholesterol |                       |                       |                        |                 |
| arithmetic mean (standard deviation)        | 4 (± 13)              | 5 (± 16)              | 7 (± 16)               | 1 (± 14)        |

| End point values                            | Evolocumab<br>140 mg |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                          | Reporting group      |  |  |  |
| Number of subjects analysed                 | 51                   |  |  |  |
| Units: Percentage change of HDL-cholesterol |                      |  |  |  |
| arithmetic mean (standard deviation)        | 5 (± 14)             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in very low-density lipoprotein (VLDL)-cholesterol

|  |   |
|--|---|
| End point title  | Change in very low-density lipoprotein (VLDL)-cholesterol |
| End point description:   |   |
| Percentage change in VLDL-cholesterol (measured in mmol/L) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Overall number of subjects analyzed = subjects with available data for this endpoint. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| From baseline (week 0) to visit 9 (week 12)  |   |

| End point values                             | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|--|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed                  | 52                    | 52                    | 50                     | 53              |
| Units: Percentage change of VLDL cholesterol |                       |                       |                        |                 |
| arithmetic mean (standard deviation)         | 5 (± 27)              | -7 (± 33)             | -15 (± 26)             | 3 (± 41)        |

| End point values                             | Evolocumab<br>140 mg |  |  |  |
|--|----------------------|--|--|--|
| Subject group type                           | Reporting group      |  |  |  |
| Number of subjects analysed                  | 52                   |  |  |  |
| Units: Percentage change of VLDL cholesterol |                      |  |  |  |
| arithmetic mean (standard deviation)         | -16 (± 24)           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in triglycerides

|  |                         |
|--|-------------------------|
| End point title  | Change in triglycerides |
| End point description:   |                         |
| Percentage change in triglycerides (measured in mg/dL) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Overall number of subjects analyzed = subjects with available data for this endpoint. |                         |
| End point type   | Secondary               |
| End point timeframe:   |                         |
| From baseline (week 0) to visit 9 (week 12)  |                         |

| End point values                          | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|---|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                        | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed               | 52                    | 52                    | 50                     | 53              |
| Units: Percentage change of triglycerides |                       |                       |                        |                 |
| arithmetic mean (standard deviation)      | 5 (± 27)              | -7 (± 31)             | -16 (± 27)             | 2 (± 41)        |

| End point values                          | Evolocumab<br>140 mg |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                        | Reporting group      |  |  |  |
| Number of subjects analysed               | 52                   |  |  |  |
| Units: Percentage change of triglycerides |                      |  |  |  |
| arithmetic mean (standard deviation)      | -16 (± 23)           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in total Apolipoprotein B (Apo B)

|                 |  |
|-----------------|--|
| End point title | Change in total Apolipoprotein B (Apo B) |
|-----------------|--|

End point description:

Percentage change in Apo B (measured in mg/dL) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Overall number of subjects analyzed = subjects with available data for this endpoint.

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

End point timeframe:

From baseline (week 0) to visit 9 (week 12)

| End point values                     | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|--------------------------------------|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 51                    | 52                    | 49                     | 53              |
| Units: Percentage change of Apo B    |                       |                       |                        |                 |
| arithmetic mean (standard deviation) | -20 (± 15)            | -34 (± 28)            | -48 (± 12)             | 6 (± 31)        |

| End point values            | Evolocumab<br>140 mg |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Reporting group      |  |  |  |
| Number of subjects analysed | 53                   |  |  |  |

|                                      |            |  |  |  |
|--------------------------------------|------------|--|--|--|
| Units: Percentage change of Apo B    |            |  |  |  |
| arithmetic mean (standard deviation) | -52 (± 17) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in total Apolipoprotein CIII (Apo CIII)

|                 |  |
|-----------------|--|
| End point title | Change in total Apolipoprotein CIII (Apo CIII) |
|-----------------|--|

End point description:

Percentage change in Apo CIII (measured in mg/dL) at week 12 is presented. Data is reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Overall number of subjects analyzed = subjects with available data for this endpoint.

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

End point timeframe:

From baseline (week 0) to visit 9 (week 12)

| End point values                     | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|--------------------------------------|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 50                    | 52                    | 48                     | 51              |
| Units: Percentage change of Apo CIII |                       |                       |                        |                 |
| arithmetic mean (standard deviation) | -0 (± 20)             | -7 (± 24)             | -16 (± 15)             | 2 (± 23)        |

| End point values                     | Evolocumab<br>140 mg |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 52                   |  |  |  |
| Units: Percentage change of Apo CIII |                      |  |  |  |
| arithmetic mean (standard deviation) | -15 (± 21)           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in total lipoprotein(a) (Lp[a])

|                 |  |
|-----------------|--|
| End point title | Change in total lipoprotein(a) (Lp[a]) |
|-----------------|--|

End point description:

Change in total Lp(a) (measured in mg/dL) at week 12 is presented as ratio to baseline. Data is

reported for the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. FAS included all randomized subjects. Overall number of subjects analyzed = subjects with available data for this endpoint.

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

End point timeframe:

From baseline (week 0) to visit 9 (week 12)

| End point values                                    | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
|---|-----------------------|-----------------------|------------------------|-----------------|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed                         | 52                    | 52                    | 50                     | 53              |
| Units: Ratio of Lipoprotein (a)                     |                       |                       |                        |                 |
| geometric mean (geometric coefficient of variation) | 0.79 (± 34.2)         | 0.70 (± 37.6)         | 0.66 (± 40.0)          | 0.99 (± 31.5)   |

| End point values                                    | Evolocumab<br>140 mg |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                                  | Reporting group      |  |  |  |
| Number of subjects analysed                         | 53                   |  |  |  |
| Units: Ratio of Lipoprotein (a)                     |                      |  |  |  |
| geometric mean (geometric coefficient of variation) | 0.59 (± 43.4)        |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Treatment-emergent adverse events (TEAEs)

|                 |   |
|-----------------|---|
| End point title | Treatment-emergent adverse events (TEAEs) |
|-----------------|---|

End point description:

An adverse events (AE) is any untoward medical occurrence in a clinical trial subject that is temporally associated with the use of an investigational medicinal product (IMP), whether or not considered related to the IMP. All presented AEs are TEAEs. TEAEs was the number of AEs recorded during the on-treatment period. The on-treatment period is the time period where subjects were considered exposed to trial product. The observation period starts at the date of first dose of trial product and ends at the first date of any of the following: The follow-up visit or the last date on randomised treatment regimen + 58 days or the end-date for the 'in-trial' observation period. Safety analysis set (SAS) included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product.

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

End point timeframe:

From baseline (week 0) to visit 10 (19 weeks + 4 days)

|                             |                       |                       |                        |                 |
|-----------------------------|-----------------------|-----------------------|------------------------|-----------------|
| <b>End point values</b>     | NNC0385-0434<br>15 mg | NNC0385-0434<br>40 mg | NNC0385-0434<br>100 mg | Placebo         |
| Subject group type          | Reporting group       | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed | 53                    | 53                    | 53                     | 54              |
| Units: Events               | 82                    | 60                    | 65                     | 56              |

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| <b>End point values</b>     | Evolocumab<br>140 mg |  |  |  |
| Subject group type          | Reporting group      |  |  |  |
| Number of subjects analysed | 54                   |  |  |  |
| Units: Events               | 81                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline (week 0) to visit 10 (19 weeks + 4 days)

Adverse event reporting additional description:

All presented AEs are TEAEs. TEAEs are AEs recorded during the on-treatment period. SAS included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 25 |
|--------------------|----|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | NNC0385-0434 15 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received 15 milligrams (mg) NNC0385-0434 (co-formulated with 500 mg salcaprozate sodium [SNAC]) tablet orally once daily for 12 weeks.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | NNC0385-0434 40 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received 40 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Evolocumab 140 mg |
|-----------------------|-------------------|

Reporting group description:

Subjects received 140 mg evolocumab injection s.c. once every weeks for 12 weeks.

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

Reporting group description:

Subjects received placebo matched to NNC0385-0434 (without SNAC) tablet orally once daily for 12 weeks.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | NNC0385-0434 100 mg |
|-----------------------|---------------------|

Reporting group description:

Subjects received 100 mg NNC0385-0434 (co-formulated with 500 mg SNAC) tablet orally once daily for 12 weeks.

| Serious adverse events  | NNC0385-0434 15 mg | NNC0385-0434 40 mg | Evolocumab 140 mg |
|---|--------------------|--------------------|-------------------|
| Total subjects affected by serious adverse events                   |                    |                    |                   |
| subjects affected / exposed   | 1 / 53 (1.89%)     | 3 / 53 (5.66%)     | 3 / 54 (5.56%)    |
| 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) |                    |                    |                   |
| Oesophageal adenocarcinoma  |                    |                    |                   |
| subjects affected / exposed   | 1 / 53 (1.89%)     | 0 / 53 (0.00%)     | 0 / 54 (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             |
| Vascular disorders  |                    |                    |                   |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Peripheral artery aneurysm                           |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 1 / 53 (1.89%) | 0 / 54 (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          |
| Cardiac disorders                                    |                |                |                |
| Diastolic dysfunction                                |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 0 / 54 (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          |
| Coronary artery stenosis                             |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ventricular tachycardia                              |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                             |                |                |                |
| Loss of consciousness                                |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Myelopathy   |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 0 / 54 (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 |                |                |                |
| Chest discomfort                                     |                |                |                |
| subjects affected / exposed                          | 0 / 53 (0.00%) | 1 / 53 (1.89%) | 0 / 54 (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          |
| Non-cardiac chest pain                               |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                            | 0 / 53 (0.00%) | 1 / 53 (1.89%) | 0 / 54 (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          |
| <b>Gastrointestinal disorders</b>                      |                |                |                |
| Dysphagia  |                |                |                |
| subjects affected / exposed                            | 1 / 53 (1.89%) | 0 / 53 (0.00%) | 0 / 54 (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          |
| <b>Hepatobiliary disorders</b>                         |                |                |                |
| Biliary colic  |                |                |                |
| subjects affected / exposed                            | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 1 / 54 (1.85%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Skin and subcutaneous tissue disorders</b>          |                |                |                |
| Urticaria  |                |                |                |
| subjects affected / exposed                            | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 0 / 54 (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          |
| <b>Musculoskeletal and connective tissue disorders</b> |                |                |                |
| Musculoskeletal chest pain                             |                |                |                |
| subjects affected / exposed                            | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 0 / 54 (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          |
| Pain in extremity                                      |                |                |                |
| subjects affected / exposed                            | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 0 / 54 (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          |
| <b>Infections and infestations</b>                     |                |                |                |
| Herpes zoster  |                |                |                |
| subjects affected / exposed                            | 0 / 53 (0.00%) | 0 / 53 (0.00%) | 0 / 54 (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          |

|                                    |         |                     |  |
|------------------------------------|---------|---------------------|--|
| <b>Serious adverse events</b>      | Placebo | NNC0385-0434 100 mg |  |
| Total subjects affected by serious |         |                     |  |

|   |                |                |  |
|---|----------------|----------------|--|
| adverse events  |                |                |  |
| subjects affected / exposed   | 5 / 54 (9.26%) | 1 / 53 (1.89%) |  |
| 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) |                |                |  |
| Oesophageal adenocarcinoma  |                |                |  |
| subjects affected / exposed   | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Vascular disorders  |                |                |  |
| Peripheral artery aneurysm  |                |                |  |
| subjects affected / exposed   | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Cardiac disorders   |                |                |  |
| Diastolic dysfunction   |                |                |  |
| subjects affected / exposed   | 1 / 54 (1.85%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Coronary artery stenosis  |                |                |  |
| subjects affected / exposed   | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Ventricular tachycardia   |                |                |  |
| subjects affected / exposed   | 0 / 54 (0.00%) | 0 / 53 (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  |                |                |  |
| Loss of consciousness   |                |                |  |
| subjects affected / exposed   | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Myelopathy  |                |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 54 (0.00%) | 1 / 53 (1.89%) |  |
| 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 |                |                |  |
| Chest discomfort                                     |                |                |  |
| subjects affected / exposed                          | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Non-cardiac chest pain                               |                |                |  |
| subjects affected / exposed                          | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                           |                |                |  |
| Dysphagia  |                |                |  |
| subjects affected / exposed                          | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                              |                |                |  |
| Biliary colic  |                |                |  |
| subjects affected / exposed                          | 0 / 54 (0.00%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Skin and subcutaneous tissue disorders               |                |                |  |
| Urticaria  |                |                |  |
| subjects affected / exposed                          | 1 / 54 (1.85%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders      |                |                |  |
| Musculoskeletal chest pain                           |                |                |  |
| subjects affected / exposed                          | 1 / 54 (1.85%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Pain in extremity                                    |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 54 (1.85%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Infections and infestations</b>              |                |                |  |
| Herpes zoster                                   |                |                |  |
| subjects affected / exposed                     | 1 / 54 (1.85%) | 0 / 53 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | NNC0385-0434 15 mg | NNC0385-0434 40 mg | Evolocumab 140 mg |
|---|--------------------|--------------------|-------------------|
| Total subjects affected by non-serious adverse events |                    |                    |                   |
| subjects affected / exposed                           | 16 / 53 (30.19%)   | 14 / 53 (26.42%)   | 17 / 54 (31.48%)  |
| <b>Investigations</b>                                 |                    |                    |                   |
| Blood creatine phosphokinase increased                |                    |                    |                   |
| subjects affected / exposed                           | 1 / 53 (1.89%)     | 0 / 53 (0.00%)     | 1 / 54 (1.85%)    |
| occurrences (all)                                     | 1                  | 0                  | 1                 |
| <b>Vascular disorders</b>                             |                    |                    |                   |
| Hypertension  |                    |                    |                   |
| subjects affected / exposed                           | 0 / 53 (0.00%)     | 1 / 53 (1.89%)     | 5 / 54 (9.26%)    |
| occurrences (all)                                     | 0                  | 1                  | 5                 |
| <b>Nervous system disorders</b>                       |                    |                    |                   |
| Headache  |                    |                    |                   |
| subjects affected / exposed                           | 4 / 53 (7.55%)     | 0 / 53 (0.00%)     | 3 / 54 (5.56%)    |
| occurrences (all)                                     | 4                  | 0                  | 3                 |
| <b>Gastrointestinal disorders</b>                     |                    |                    |                   |
| Diarrhoea   |                    |                    |                   |
| subjects affected / exposed                           | 4 / 53 (7.55%)     | 4 / 53 (7.55%)     | 1 / 54 (1.85%)    |
| occurrences (all)                                     | 4                  | 4                  | 1                 |
| Constipation  |                    |                    |                   |
| subjects affected / exposed                           | 3 / 53 (5.66%)     | 0 / 53 (0.00%)     | 0 / 54 (0.00%)    |
| occurrences (all)                                     | 3                  | 0                  | 0                 |
| Nausea  |                    |                    |                   |
| subjects affected / exposed                           | 1 / 53 (1.89%)     | 3 / 53 (5.66%)     | 0 / 54 (0.00%)    |
| occurrences (all)                                     | 1                  | 4                  | 0                 |

|  |  |   |   |
|--|--|---|---|
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 53 (1.89%)<br>2                            | 0 / 53 (0.00%)<br>0                             | 1 / 54 (1.85%)<br>1                             |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 53 (0.00%)<br>0                            | 0 / 53 (0.00%)<br>0                             | 3 / 54 (5.56%)<br>3                             |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 3 / 53 (5.66%)<br>4                            | 0 / 53 (0.00%)<br>0                             | 2 / 54 (3.70%)<br>2                             |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 3 / 53 (5.66%)<br>3<br><br>1 / 53 (1.89%)<br>1 | 8 / 53 (15.09%)<br>8<br><br>3 / 53 (5.66%)<br>4 | 6 / 54 (11.11%)<br>6<br><br>0 / 54 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>  | Placebo             | NNC0385-0434 100 mg |  |
|--|---------------------|---------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                         | 14 / 54 (25.93%)    | 19 / 53 (35.85%)    |  |
| Investigations<br>Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all) | 4 / 54 (7.41%)<br>4 | 3 / 53 (5.66%)<br>3 |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 54 (0.00%)<br>0 | 1 / 53 (1.89%)<br>1 |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 54 (3.70%)<br>2 | 0 / 53 (0.00%)<br>0 |  |
| Gastrointestinal disorders<br>Diarrhoea  |                     |                     |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 54 (0.00%)<br>0  | 2 / 53 (3.77%)<br>5  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 1 / 54 (1.85%)<br>1  | 0 / 53 (0.00%)<br>0  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 54 (0.00%)<br>0  | 3 / 53 (5.66%)<br>3  |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 54 (0.00%)<br>0  | 3 / 53 (5.66%)<br>4  |  |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 54 (0.00%)<br>0  | 0 / 53 (0.00%)<br>0  |  |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all)            | 2 / 54 (3.70%)<br>2  | 0 / 53 (0.00%)<br>0  |  |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)                               | 6 / 54 (11.11%)<br>6 | 8 / 53 (15.09%)<br>8 |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 3 / 54 (5.56%)<br>3  | 2 / 53 (3.77%)<br>2  |  |

## 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