



Clinical trial results:

Investigation of the safety and efficacy of semaglutide s.c. in combination with NNC0480-0389 in participants with type 2 diabetes-a dose finding study.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2020-004863-14 |
| Trial protocol | DK HU GR BG |
| Global end of trial date | 23 March 2023 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 07 April 2024 |
| First version publication date | 07 April 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | NN9389-4606 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05144984 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Japanese trial registration: jRCT2031210474 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novo Nordisk A/S |
| Sponsor organisation address | Novo Alle, 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 | 02 June 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 March 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate superiority of subcutaneously co administered semaglutide and NNC0480-0389 (in different dose ratios) versus placebo on change in HbA1c from baseline to week 34 in subjects with Type 2 Diabetes inadequately controlled on diet and exercise with or without metformin.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki last amended by the 64th World Medical Association General Assembly, October 2013 and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents, E6(R2), Current step 4 version, 09 November 2016 and 21 CFR 312.120.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

| | |
|---|------------------|
| Actual start date of recruitment | 29 November 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Bulgaria: 55 |
| Country: Number of subjects enrolled | Denmark: 18 |
| Country: Number of subjects enrolled | Greece: 57 |
| Country: Number of subjects enrolled | Hungary: 74 |
| Country: Number of subjects enrolled | Japan: 55 |
| Country: Number of subjects enrolled | Poland: 87 |
| Country: Number of subjects enrolled | Russian Federation: 7 |
| Country: Number of subjects enrolled | Serbia: 28 |
| Country: Number of subjects enrolled | United States: 119 |
| Worldwide total number of subjects | 500 |
| EEA total number of subjects | 291 |

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) | 353 |
| From 65 to 84 years | 147 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The trial was conducted in 9 countries (86 sites screened/83 randomised subjects): Bulgaria: 6/6; Denmark: 3/3; Greece: 7/7; Hungary: 9/9; Japan: 6/6; Poland: 10/10; Russia: 4/4; Serbia: 3/3; United States of America (USA): 38/35.

Pre-assignment

Screening details:

The trial had a 34-week intervention period (10 weeks of dose escalation period and followed by two 12-week maintenance period), followed by a 5-week follow-up period.

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, Carer, Assessor |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg |

Arm description:

Subjects received once weekly 2.4 milligram (mg) semaglutide co-administered with 2.4 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/0.5 mg from week 2 to week 6, 1.0 mg/1.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/2.0 mg from week 10 to week 22) and (2.4 mg/ 2.4 mg from week 22 to week 34).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NNC0480-0389 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received once weekly 2.4 mg NNC0480-0389 subcutaneously for 34 weeks.

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

Dosage and administration details:

Subjects received once weekly 2.4 mg semaglutide subcutaneously for 34 weeks.

| | |
|------------------|--|
| Arm title | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg |
|------------------|--|

Arm description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 7.2 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.8 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/1.5 mg from week 2 to week 6, 1.0 mg/3.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/6.0 mg from week 10 to week 22) and (2.4 mg/ 7.2 mg from week 22 to week 34).

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

| | |
|--|------------------------|
| Investigational medicinal product name | NNC0480-0389 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received once weekly 7.2 mg NNC0480-0389 subcutaneously for 34 weeks.

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

Dosage and administration details:

Subjects received once weekly 2.4 mg semaglutide subcutaneously for 34 weeks.

| | |
|------------------|---|
| Arm title | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|------------------|---|

Arm description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 12.0 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/1.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/2.5 mg from week 2 to week 6, 1.0 mg/5.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/10.0 mg from week 10 to week 22) and (2.4 mg/ 12.0 mg from week 22 to week 34).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NNC0480-0389 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Subjects received once weekly 12.0 mg NNC0480-0389 subcutaneously for 34 weeks.

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

Dosage and administration details:

Subjects received once weekly 2.4mg semaglutide subcutaneously for 34 weeks.

| | |
|------------------|---|
| Arm title | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|------------------|---|

Arm description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 21.6 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/2.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/4.5 mg from week 2 to week 6, 1.0 mg/9.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/18.0 mg from week 10 to week 22) and (2.4 mg/ 21.6 mg from week 22 to week 34).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NNC0480-0389 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

| | |
|---|--|
| Dosage and administration details: | |
| Subjects received once weekly 21.6 mg NNC0480-0389 subcutaneously for 34 weeks. | |
| Investigational medicinal product name | Semaglutide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Subjects received once weekly 2.4mg semaglutide subcutaneously for 34 weeks. | |
| Arm title | Semaglutide 2.4 mg + placebo (NNC0480-0389) |
| Arm description: | |
| Subjects received once weekly 2.4 mg semaglutide co-administered with placebo matched to NNC0480-0389 subcutaneously for 34 weeks. | |
| Arm type | Placebo |
| Investigational medicinal product name | Semaglutide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Subjects received once weekly 2.4 mg semaglutide subcutaneously for 34 weeks. | |
| Investigational medicinal product name | Placebo (NNC0480-0389) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Subjects received once weekly placebo (NNC0480-0389) subcutaneously for 34 weeks. | |
| Arm title | NNC0480-0389 21.6 mg + placebo (semaglutide) |
| Arm description: | |
| Subjects received once weekly 21.6 mg NNC0480-0389 co-administered with placebo matched to semaglutide subcutaneously for 34 weeks. | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo (semaglutide) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Subjects received once weekly placebo (semaglutide) subcutaneously for 34 weeks. | |
| Investigational medicinal product name | NNC0480-0389 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Subjects received once weekly 21.6 mg NNC0480-0389 subcutaneously for 34 weeks. | |
| Arm title | Placebo |
| Arm description: | |
| Subjects received subcutaneous dose of semaglutide matched placebo and NNC0480-0389 matched placebo once weekly for 34 weeks. | |
| 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:

Subjects received once weekly subcutaneous dose of semaglutide matched placebo and NNC0480-0389 matched placebo for 34 weeks.

| Number of subjects in period 1 | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|---------------------------------------|--|--|---|
| Started | 77 | 74 | 77 |
| Exposed | 77 | 74 | 77 |
| Full Analysis Set (FAS) | 77 | 74 | 77 |
| Safety Analysis Set (SAS) | 77 | 74 | 77 |
| Completed | 74 | 72 | 74 |
| Not completed | 3 | 2 | 3 |
| Consent withdrawn by subject | 2 | - | 2 |
| Investigator decision | 1 | - | - |
| Lost to follow-up | - | 2 | 1 |

| Number of subjects in period 1 | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) |
|---------------------------------------|---|---|--|
| Started | 77 | 75 | 59 |
| Exposed | 77 | 75 | 59 |
| Full Analysis Set (FAS) | 77 | 75 | 59 |
| Safety Analysis Set (SAS) | 77 | 75 | 59 |
| Completed | 74 | 72 | 57 |
| Not completed | 3 | 3 | 2 |
| Consent withdrawn by subject | 3 | - | 2 |
| Investigator decision | - | - | - |
| Lost to follow-up | - | 3 | - |

| Number of subjects in period 1 | Placebo |
|---------------------------------------|---------|
| Started | 61 |
| Exposed | 61 |
| Full Analysis Set (FAS) | 61 |
| Safety Analysis Set (SAS) | 61 |
| Completed | 59 |
| Not completed | 2 |
| Consent withdrawn by subject | 2 |
| Investigator decision | - |

| | |
|-------------------|---|
| Lost to follow-up | - |
|-------------------|---|

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg |
| Reporting group description: Subjects received once weekly 2.4 milligram (mg) semaglutide co-administered with 2.4 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/0.5 mg from week 2 to week 6, 1.0 mg/1.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/2.0 mg from week 10 to week 22) and (2.4 mg/ 2.4 mg from week 22 to week 34). | |
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg |
| Reporting group description: Subjects received once weekly 2.4 mg semaglutide co-administered with 7.2 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.8 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/1.5 mg from week 2 to week 6, 1.0 mg/3.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/6.0 mg from week 10 to week 22) and (2.4 mg/ 7.2 mg from week 22 to week 34). | |
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
| Reporting group description: Subjects received once weekly 2.4 mg semaglutide co-administered with 12.0 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/1.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/2.5 mg from week 2 to week 6, 1.0 mg/5.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/10.0 mg from week 10 to week 22) and (2.4 mg/ 12.0 mg from week 22 to week 34). | |
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Reporting group description: Subjects received once weekly 2.4 mg semaglutide co-administered with 21.6 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/2.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/4.5 mg from week 2 to week 6, 1.0 mg/9.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/18.0 mg from week 10 to week 22) and (2.4 mg/ 21.6 mg from week 22 to week 34). | |
| Reporting group title | Semaglutide 2.4 mg + placebo (NNC0480-0389) |
| Reporting group description: Subjects received once weekly 2.4 mg semaglutide co-administered with placebo matched to NNC0480-0389 subcutaneously for 34 weeks. | |
| Reporting group title | NNC0480-0389 21.6 mg + placebo (semaglutide) |
| Reporting group description: Subjects received once weekly 21.6 mg NNC0480-0389 co-administered with placebo matched to semaglutide subcutaneously for 34 weeks. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received subcutaneous dose of semaglutide matched placebo and NNC0480-0389 matched placebo once weekly for 34 weeks. | |

| Reporting group values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|------------------------|--|--|---|
| Number of subjects | 77 | 74 | 77 |

| | | | |
|---------------------------------------|------|------|------|
| Age Categorical Units: Subjects | | | |
| Adults (18-64 years) | 47 | 57 | 58 |
| From 65-84 years | 30 | 17 | 19 |
| Age Continuous Units: years | | | |
| arithmetic mean | 59 | 57 | 58 |
| standard deviation | ± 11 | ± 10 | ± 10 |
| Gender Categorical Units: Subjects | | | |
| Female | 26 | 33 | 25 |
| Male | 51 | 41 | 52 |

| | | | |
|---------------------------------------|---|---|--|
| Reporting group values | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) |
| Number of subjects | 77 | 75 | 59 |
| Age Categorical Units: Subjects | | | |
| Adults (18-64 years) | 53 | 53 | 41 |
| From 65-84 years | 24 | 22 | 18 |
| Age Continuous Units: years | | | |
| arithmetic mean | 59 | 58 | 57 |
| standard deviation | ± 9 | ± 9 | ± 10 |
| Gender Categorical Units: Subjects | | | |
| Female | 38 | 27 | 22 |
| Male | 39 | 48 | 37 |

| | | | |
|---------------------------------------|---------|-------|--|
| Reporting group values | Placebo | Total | |
| Number of subjects | 61 | 500 | |
| Age Categorical Units: Subjects | | | |
| Adults (18-64 years) | 44 | 353 | |
| From 65-84 years | 17 | 147 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 58 | - | |
| standard deviation | ± 9 | - | |
| Gender Categorical Units: Subjects | | | |
| Female | 27 | 198 | |
| Male | 34 | 302 | |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg |
|-----------------------|--|

Reporting group description:

Subjects received once weekly 2.4 milligram (mg) semaglutide co-administered with 2.4 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/0.5 mg from week 2 to week 6, 1.0 mg/1.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/2.0 mg from week 10 to week 22) and (2.4 mg/ 2.4 mg from week 22 to week 34).

| | |
|-----------------------|--|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg |
|-----------------------|--|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 7.2 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.8 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/1.5 mg from week 2 to week 6, 1.0 mg/3.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/6.0 mg from week 10 to week 22) and (2.4 mg/ 7.2 mg from week 22 to week 34).

| | |
|-----------------------|---|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|-----------------------|---|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 12.0 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/1.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/2.5 mg from week 2 to week 6, 1.0 mg/5.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/10.0 mg from week 10 to week 22) and (2.4 mg/ 12.0 mg from week 22 to week 34).

| | |
|-----------------------|---|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|-----------------------|---|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 21.6 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/2.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/4.5 mg from week 2 to week 6, 1.0 mg/9.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/18.0 mg from week 10 to week 22) and (2.4 mg/ 21.6 mg from week 22 to week 34).

| | |
|-----------------------|---|
| Reporting group title | Semaglutide 2.4 mg + placebo (NNC0480-0389) |
|-----------------------|---|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with placebo matched to NNC0480-0389 subcutaneously for 34 weeks.

| | |
|-----------------------|--|
| Reporting group title | NNC0480-0389 21.6 mg + placebo (semaglutide) |
|-----------------------|--|

Reporting group description:

Subjects received once weekly 21.6 mg NNC0480-0389 co-administered with placebo matched to semaglutide subcutaneously for 34 weeks.

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

Reporting group description:

Subjects received subcutaneous dose of semaglutide matched placebo and NNC0480-0389 matched placebo once weekly for 34 weeks.

Primary: Change in HbA1c

| | |
|---|-----------------|
| End point title | Change in HbA1c |
| End point description: Change from baseline at week 0 to week 34 in HbA1c is presented. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. Full Analysis Set (FAS) FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis. | |
| End point type | Primary |
| End point timeframe: From baseline (week 0) to visit 24 (week 34) | |

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|--------------------------------------|--|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 | 74 | 77 | 77 |
| Units: Percentage point of HbA1c | | | | |
| arithmetic mean (standard deviation) | -2.3 (± 0.9) | -2.2 (± 0.8) | -2.2 (± 1.1) | -2.3 (± 1.0) |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|--------------------------------------|---|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 59 | 61 | |
| Units: Percentage point of HbA1c | | | | |
| arithmetic mean (standard deviation) | -2.3 (± 0.9) | -1.1 (± 1.1) | -0.4 (± 1.2) | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | 2.4 mg semaglutide + 2.4 mg 0389, Placebo |
| Statistical analysis description: Hypothetical estimand | |
| Comparison groups | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg v Placebo |
| Number of subjects included in analysis | 138 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Estimated treatment difference |
| Point estimate | -1.9 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.3 |
| upper limit | -1.4 |

Notes:

[1] - Responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline HbA1c as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.

| | |
|-----------------------------------|--|
| Statistical analysis title | 2.4 mg semaglutide + 21.6 mg 0389 vs Placebo |
|-----------------------------------|--|

Statistical analysis description:

Hypothetical estimand

| | |
|---|---|
| Comparison groups | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg v Placebo |
| Number of subjects included in analysis | 138 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Estimated treatment difference |
| Point estimate | -1.9 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | -1.5 |

Notes:

[2] - Responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline HbA1c as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.

| | |
|-----------------------------------|--|
| Statistical analysis title | 2.4 mg semaglutide + 12.0 mg NNC0480-0389, Placebo |
|-----------------------------------|--|

Statistical analysis description:

Hypothetical estimand

| | |
|---|---|
| Comparison groups | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg v Placebo |
| Number of subjects included in analysis | 138 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Estimated treatment difference |
| Point estimate | -1.9 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | -1.5 |

Notes:

[3] - Responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline HbA1c as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.

| | |
|-----------------------------------|---|
| Statistical analysis title | 2.4 mg semaglutide + 7.2 mg NNC0480-0389, Placebo |
|-----------------------------------|---|

Statistical analysis description:

Hypothetical estimand

| | |
|---|--|
| Comparison groups | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg v Placebo |
| Number of subjects included in analysis | 135 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Estimated treatment difference |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | -1.5 |

Notes:

[4] - Responses were analysed using an analysis of covariance model with randomised treatment and strata as factors and baseline HbA1c as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.

Secondary: Change in body weight (kg)

| | |
|-----------------|----------------------------|
| End point title | Change in body weight (kg) |
|-----------------|----------------------------|

End point description:

Change from baseline at week 0 to week 34 in body weight is presented. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

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

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|--------------------------------------|--|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 60 | 65 | 65 |
| Units: Kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | -8.9 (± 5.8) | -12 (± 7.7) | -10 (± 5.9) | -12 (± 5.4) |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|--------------------------------------|---|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 60 | 43 | 37 | |
| Units: Kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | -9.8 (± 5.8) | -4.7 (± 5.1) | -2.6 (± 3.9) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose

End point title Change in fasting plasma glucose

End point description:

Change from baseline at week 0 to week 34 in Fasting Plasma Glucose (FPG) is presented. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

End point type Secondary

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 58 | 63 | 63 |
| Units: millimoles per litre (mmol/L) | | | | |
| arithmetic mean (standard deviation) | -3.9 (± 2.6) | -3.4 (± 2.1) | -3.8 (± 2.4) | -3.8 (± 2.9) |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|--------------------------------------|--|---|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 43 | 36 | |
| Units: millimoles per litre (mmol/L) | | | | |
| arithmetic mean (standard deviation) | -3.6 (± 1.8) | -1.4 (± 2.8) | -0.1 (± 3.2) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight (%)

| | |
|---|---------------------------|
| End point title | Change in body weight (%) |
| End point description: | |
| Change from baseline at week 0 to week 34 in body weight is presented. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline (week 0) to visit 24 (week 34) | |

| | | | | |
|--------------------------------------|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 60 | 65 | 65 |
| Units: Percentage of body weight | | | | |
| arithmetic mean (standard deviation) | -9.3 (± 5.8) | -13 (± 7.3) | -11 (± 5.8) | -13 (± 5.4) |

| | | | | |
|--------------------------------------|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 60 | 43 | 37 | |
| Units: Percentage of body weight | | | | |
| arithmetic mean (standard deviation) | -10 (± 6.3) | -4.3 (± 4.5) | -2.7 (± 4.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in waist circumference

| | |
|---|-------------------------------|
| End point title | Change in waist circumference |
| End point description: | |
| Change from baseline at week 0 to week 34 in waist circumference is presented. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline (week 0) to visit 24 (week 34) | |

| | | | | |
|--------------------------------------|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 60 | 65 | 65 |
| Units: Centimeter (cm) | | | | |
| arithmetic mean (standard deviation) | -8 (± 5) | -11 (± 7) | -9 (± 7) | -10 (± 7) |

| | | | | |
|--------------------------------------|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 60 | 43 | 37 | |
| Units: Centimeter (cm) | | | | |
| arithmetic mean (standard deviation) | -8 (± 6) | -5 (± 5) | -3 (± 5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in systolic blood pressure (SBP)

| | |
|-----------------|---|
| End point title | Change in systolic blood pressure (SBP) |
|-----------------|---|

End point description:

Change from baseline at week 0 to week 34 in systolic blood pressure is presented. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

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

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| | | | | |
|--------------------------------------|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 60 | 65 | 65 |
| Units: Millimeters of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | -6 (± 12) | -10 (± 14) | -9 (± 13) | -13 (± 12) |

| | | | | |
|--------------------------------------|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 60 | 43 | 37 | |
| Units: Millimeters of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | -5 (± 16) | -3 (± 12) | 0 (± 8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in total cholesterol

| | |
|---|--------------------------------------|
| End point title | Relative change in total cholesterol |
| End point description: | |
| Change from baseline at week 0 to week 34 in total cholesterol measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline (week 0) to visit 24 (week 34) | |

| | | | | |
|---|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 56 | 64 | 64 |
| Units: Ratio of total cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 0.94 (± 19.7) | 0.89 (± 22.7) | 0.90 (± 21.7) | 0.90 (± 17.3) |

| | | | | |
|-----------------------------------|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 42 | 36 | |
| Units: Ratio of total cholesterol | | | | |

| | | | | |
|---|---------------|---------------|---------------|--|
| geometric mean (geometric coefficient of variation) | 0.93 (± 18.2) | 1.00 (± 22.9) | 0.96 (± 16.2) | |
|---|---------------|---------------|---------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in HDL cholesterol

| | |
|-----------------|------------------------------------|
| End point title | Relative change in HDL cholesterol |
|-----------------|------------------------------------|

End point description:

Change from baseline at week 0 to week 34 in High-Density Lipoprotein (HDL) cholesterol measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

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

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|---|--|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 57 | 62 | 64 |
| Units: Ratio of HDL cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 1.05 (± 17.6) | 1.06 (± 19.8) | 1.07 (± 16.7) | 1.00 (± 16.0) |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|---|---|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 42 | 35 | |
| Units: Ratio of HDL cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 1.04 (± 15.6) | 1.04 (± 16.2) | 1.04 (± 17.0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in LDL cholesterol

End point title Relative change in LDL cholesterol

End point description:

Change from baseline at week 0 to week 34 in Low-Density Lipoprotein (LDL) cholesterol measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

End point type Secondary

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|---|--|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 56 | 61 | 63 |
| Units: Ratio of LDL cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 0.95 (± 28.4) | 0.85 (± 46.5) | 0.91 (± 37.5) | 0.88 (± 36.0) |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|---|---|--|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 58 | 41 | 34 | |
| Units: Ratio of LDL cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 0.95 (± 32.2) | 0.96 (± 53.5) | 0.96 (± 29.8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in VLDL cholesterol

End point title Relative change in VLDL cholesterol

End point description:

Change from baseline at week 0 to week 34 in Very-Low-Density Lipoprotein (VLDL) cholesterol measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From baseline (week 0) to visit 24 (week 34) | |

| | | | | |
|---|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 56 | 62 | 64 |
| Units: Ratio of VLDL cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 0.75 (± 54.0) | 0.76 (± 46.4) | 0.72 (± 48.9) | 0.78 (± 48.2) |

| | | | | |
|---|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 42 | 35 | |
| Units: Ratio of VLDL cholesterol | | | | |
| geometric mean (geometric coefficient of variation) | 0.72 (± 39.9) | 0.95 (± 47.9) | 0.86 (± 44.5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in triglycerides

| | |
|---|----------------------------------|
| End point title | Relative change in triglycerides |
| End point description: | |
| Change from baseline at week 0 to week 34 in triglycerides measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline (week 0) to visit 24 (week 34) | |

| | | | | |
|---|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 56 | 62 | 64 |
| Units: Ratio of triglycerides | | | | |
| geometric mean (geometric coefficient of variation) | 0.75 (± 53.9) | 0.76 (± 46.1) | 0.72 (± 49.1) | 0.78 (± 47.8) |

| | | | | |
|---|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 42 | 35 | |
| Units: Ratio of triglycerides | | | | |
| geometric mean (geometric coefficient of variation) | 0.72 (± 40.0) | 0.96 (± 47.8) | 0.86 (± 44.7) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in free fatty acids

| | |
|-----------------|-------------------------------------|
| End point title | Relative change in free fatty acids |
|-----------------|-------------------------------------|

End point description:

Change in baseline at week 0 to week 34 in free fatty acids measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analysed = Number of subjects contributing to the analysis.

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

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| | | | | |
|---|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 57 | 64 | 65 |
| Units: Ratio of free fatty acids | | | | |
| geometric mean (geometric coefficient of variation) | 0.85 (± 76.1) | 0.74 (± 66.0) | 0.77 (± 43.5) | 0.75 (± 64.9) |

| | | | | |
|---|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 58 | 43 | 35 | |
| Units: Ratio of free fatty acids | | | | |
| geometric mean (geometric coefficient of variation) | 0.88 (± 42.3) | 0.96 (± 51.1) | 0.91 (± 47.3) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in Apolipoprotein B

| | |
|------------------------|--|
| End point title | Relative change in Apolipoprotein B |
| End point description: | Change from baseline at week 0 to week 34 in Apolipoprotein B (Apo B) measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis. |
| End point type | Secondary |
| End point timeframe: | From baseline (week 0) to visit 24 (week 34) |

| | | | | |
|---|---|---|--|--|
| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 58 | 65 | 65 |
| Units: Ratio of ApoB | | | | |
| geometric mean (geometric coefficient of variation) | 0.90 (± 22.8) | 0.84 (± 25.7) | 0.85 (± 23.5) | 0.85 (± 22.1) |

| | | | | |
|-----------------------------|--|---|-----------------|--|
| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 43 | 36 | |

| | | | | |
|---|--------------------|--------------------|--------------------|--|
| Units: Ratio of ApoB | | | | |
| geometric mean (geometric coefficient of variation) | 0.91 (\pm 18.4) | 1.00 (\pm 28.2) | 0.94 (\pm 14.7) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in high sensitivity C-Reactive Protein (hsCRP)

| | |
|-----------------|--|
| End point title | Relative change in high sensitivity C-Reactive Protein (hsCRP) |
|-----------------|--|

End point description:

Change from baseline at week 0 to week 34 in hsCRP measured as milligrams per deciliter (mg/dL) is presented as ratio to baseline. The outcome measure was evaluated based on the data from on treatment without rescue medication. On treatment without rescue medication: the time period where all observed data for which subjects are considered exposed to randomised treatment and have not initiated any rescue medication. FAS which comprised all randomised subjects. Number of subjects analyzed = Number of subjects contributing to the analysis.

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

End point timeframe:

From baseline (week 0) to visit 24 (week 34)

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|---|--|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 57 | 64 | 65 |
| Units: Ratio of hsCRP | | | | |
| geometric mean (geometric coefficient of variation) | 0.56 (\pm 107.0) | 0.54 (\pm 136.9) | 0.64 (\pm 147.9) | 0.66 (\pm 135.5) |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|---|---|--|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 59 | 43 | 35 | |
| Units: Ratio of hsCRP | | | | |
| geometric mean (geometric coefficient of variation) | 0.61 (\pm 141.5) | 0.82 (\pm 89.7) | 0.93 (\pm 201.6) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent adverse events (TEAEs)

End point title | Number of treatment-emergent adverse events (TEAEs)

End point description:

An adverse event (AE) defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of an investigational medicinal product (IMP). All AEs mentioned are treatment emergent adverse events (TEAE) defined as an event with onset during the on treatment period. On treatment period: the time period where all observed data for which subjects are considered exposed to randomised treatment. Safety Analysis Set (SAS) included all participants exposed to randomised treatment.

End point type | Secondary

End point timeframe:

From baseline (week 0) to visit 25 (week 39)

| End point values | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 77 | 74 | 77 | 77 |
| Units: Events | | | | |
| number (not applicable) | 229 | 304 | 206 | 308 |

| End point values | Semaglutide 2.4 mg + placebo (NNC0480- 0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) | Placebo | |
|-----------------------------|--|---|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 59 | 61 | |
| Units: Events | | | | |
| number (not applicable) | 271 | 240 | 95 | |

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 25 (week 39)

Adverse event reporting additional description:

All presented AEs are TEAEs, defined as an event with onset during the on treatment period. Results are based on the SAS which included all subjects exposed to randomised treatment.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg |
|-----------------------|--|

Reporting group description:

Subjects received once weekly 2.4 milligram (mg) semaglutide co-administered with 2.4 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/0.5 mg from week 2 to week 6, 1.0 mg/1.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/2.0 mg from week 10 to week 22) and (2.4 mg/ 2.4 mg from week 22 to week 34).

| | |
|-----------------------|--|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg |
|-----------------------|--|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 7.2 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/0.8 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/1.5 mg from week 2 to week 6, 1.0 mg/3.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/6.0 mg from week 10 to week 22) and (2.4 mg/ 7.2 mg from week 22 to week 34).

| | |
|-----------------------|---|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|-----------------------|---|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 12.0 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/1.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/2.5 mg from week 2 to week 6, 1.0 mg/5.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/10.0 mg from week 10 to week 22) and (2.4 mg/ 12.0 mg from week 22 to week 34).

| | |
|-----------------------|---|
| Reporting group title | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg |
|-----------------------|---|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with 21.6 mg NNC0480-0389 subcutaneously for 34 weeks. Subjects received once weekly semaglutide co-administered with NNC0480-0389 subcutaneously in dose escalation manner for 10-weeks followed by two 12-weeks maintenance periods: (0.25 mg semaglutide/2.3 mg NNC0480-0389 from week 0 to week 2, 0.5 mg/4.5 mg from week 2 to week 6, 1.0 mg/9.0 mg from week 6 to week 10) and followed by two 12-weeks maintenance periods (2.0 mg/18.0 mg from week 10 to week 22) and (2.4 mg/ 21.6 mg from week 22 to week 34).

| | |
|-----------------------|---|
| Reporting group title | Semaglutide 2.4 mg + placebo (NNC0480-0389) |
|-----------------------|---|

Reporting group description:

Subjects received once weekly 2.4 mg semaglutide co-administered with placebo matched to NNC0480-0389 subcutaneously for 34 weeks.

| | |
|-----------------------|--|
| Reporting group title | NNC0480-0389 21.6 mg + placebo (semaglutide) |
|-----------------------|--|

Reporting group description:

Subjects received once weekly 21.6 mg NNC0480-0389 co-administered with placebo matched to semaglutide subcutaneously for 34 weeks.

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

Reporting group description:

Subjects received subcutaneous dose of semaglutide matched placebo and NNC0480-0389 matched placebo once weekly for 34 weeks.

| Serious adverse events | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|---|--|--|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 3 / 74 (4.05%) | 2 / 77 (2.60%) |
| 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) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Giant cell arteritis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Pulmonary fibrosis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Injury, poisoning and procedural complications | | | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 | | | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 occlusion subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Supraventricular tachycardia subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 Transient ischaemic attack subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIth nerve paralysis subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 / 77 (0.00%) | 0 / 74 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Pancreatic disorder | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 74 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Hepatic cirrhosis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 |
| Portal hypertension | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (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 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 |
| Endocrine disorders | | | |
| Parathyroid cyst | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 device infection | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | 0 / 77 (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 |

| Serious adverse events | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 3 / 75 (4.00%) | 2 / 59 (3.39%) |
| 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) | | | |
| Colon cancer | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 | | | |
| Giant cell arteritis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 59 (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 |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 59 (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 |
| Injury, poisoning and procedural complications | | | |
| Humerus fracture | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 59 (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 |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 disease | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 1 / 59 (1.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 59 (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 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 75 (1.33%) | 0 / 59 (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 |
| Supraventricular tachycardia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Nervous system disorders | | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Vlith nerve paralysis | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Ascites | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic disorder | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |
| Portal hypertension | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Endocrine disorders | | | |
| Parathyroid cyst | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (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 device infection | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 0 / 75 (0.00%) | 0 / 59 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Placebo | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 61 (3.28%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Giant cell arteritis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|----------------------------------|--|--|
| Non-cardiac chest pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 61 (1.64%) 0 / 1 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders Pulmonary embolism subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 61 (1.64%) 1 / 1 0 / 0 | | |
| Pulmonary fibrosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 61 (0.00%) 0 / 0 0 / 0 | | |
| Psychiatric disorders Suicide attempt subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 61 (0.00%) 0 / 0 0 / 0 | | |
| Injury, poisoning and procedural complications Humerus fracture subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 61 (0.00%) 0 / 0 0 / 0 | | |
| Cardiac disorders Atrioventricular block complete subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 61 (0.00%) 0 / 0 0 / 0 | | |
| Angina pectoris subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 61 (0.00%) 0 / 0 0 / 0 | | |
| Atrioventricular block second degree | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|----------------|--|--|
| Anaemia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatic disorder | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Portal hypertension | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Parathyroid cyst | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular device infection | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Semaglutide 2.4 mg + NNC0480-0389 2.4 mg | Semaglutide 2.4 mg + NNC0480-0389 7.2 mg | Semaglutide 2.4 mg + NNC0480-0389 12.0 mg |
|---|--|--|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 77 (51.95%) | 44 / 74 (59.46%) | 36 / 77 (46.75%) |
| Investigations | | | |
| Amylase increased | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 3 / 74 (4.05%) | 0 / 77 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 9 / 74 (12.16%) | 2 / 77 (2.60%) |
| occurrences (all) | 4 | 10 | 2 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 4 / 74 (5.41%) | 0 / 77 (0.00%) |
| occurrences (all) | 2 | 5 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 3 / 74 (4.05%) | 4 / 77 (5.19%) |
| occurrences (all) | 4 | 3 | 4 |
| Headache | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 3 / 74 (4.05%) | 5 / 77 (6.49%) |
| occurrences (all) | 9 | 3 | 7 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | 2 / 77 (2.60%) |
| occurrences (all) | 1 | 1 | 3 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | 3 / 77 (3.90%) |
| occurrences (all) | 1 | 1 | 3 |
| Injection site pruritus | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 1 | 1 / 74 (1.35%) 2 | 0 / 77 (0.00%) 0 |
| Injection site erythema subjects affected / exposed occurrences (all) | 0 / 77 (0.00%) 0 | 1 / 74 (1.35%) 1 | 4 / 77 (5.19%) 10 |
| Injection site reaction subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 1 | 2 / 74 (2.70%) 3 | 2 / 77 (2.60%) 4 |
| Gastrointestinal disorders | | | |
| Dyspepsia subjects affected / exposed occurrences (all) | 4 / 77 (5.19%) 4 | 3 / 74 (4.05%) 4 | 2 / 77 (2.60%) 2 |
| Eructation subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 2 | 2 / 74 (2.70%) 5 | 1 / 77 (1.30%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 11 / 77 (14.29%) 25 | 16 / 74 (21.62%) 30 | 11 / 77 (14.29%) 22 |
| Constipation subjects affected / exposed occurrences (all) | 4 / 77 (5.19%) 4 | 6 / 74 (8.11%) 7 | 7 / 77 (9.09%) 7 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 2 | 2 / 74 (2.70%) 2 | 2 / 77 (2.60%) 2 |
| Nausea subjects affected / exposed occurrences (all) | 15 / 77 (19.48%) 21 | 9 / 74 (12.16%) 25 | 5 / 77 (6.49%) 8 |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 77 (5.19%) 4 | 7 / 74 (9.46%) 9 | 4 / 77 (5.19%) 4 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 5 / 74 (6.76%) 5 | 3 / 77 (3.90%) 3 |
| Infections and infestations | | | |

| | | | |
|--|---------------------|----------------------|---------------------|
| COVID-19 subjects affected / exposed occurrences (all) | 6 / 77 (7.79%) 7 | 4 / 74 (5.41%) 4 | 6 / 77 (7.79%) 6 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 77 (0.00%) 0 | 2 / 74 (2.70%) 2 | 2 / 77 (2.60%) 2 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 77 (3.90%) 4 | 4 / 74 (5.41%) 4 | 4 / 77 (5.19%) 4 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 4 / 77 (5.19%) 4 | 8 / 74 (10.81%) 8 | 3 / 77 (3.90%) 4 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 1 | 0 / 74 (0.00%) 0 | 2 / 77 (2.60%) 2 |

| Non-serious adverse events | Semaglutide 2.4 mg + NNC0480-0389 21.6 mg | Semaglutide 2.4 mg + placebo (NNC0480-0389) | NNC0480-0389 21.6 mg + placebo (semaglutide) |
|---|---|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 37 / 77 (48.05%) | 34 / 75 (45.33%) | 25 / 59 (42.37%) |
| Investigations Amylase increased subjects affected / exposed occurrences (all) | 5 / 77 (6.49%) 5 | 1 / 75 (1.33%) 1 | 1 / 59 (1.69%) 1 |
| Lipase increased subjects affected / exposed occurrences (all) | 7 / 77 (9.09%) 8 | 2 / 75 (2.67%) 2 | 1 / 59 (1.69%) 1 |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 1 / 75 (1.33%) 1 | 1 / 59 (1.69%) 1 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 3 / 77 (3.90%) 4 | 5 / 75 (6.67%) 6 | 0 / 59 (0.00%) 0 |
| Headache | | | |

| | | | |
|---|------------------------|------------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 3 / 77 (3.90%) 6 | 7 / 75 (9.33%) 16 | 5 / 59 (8.47%) 12 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed occurrences (all) | 4 / 77 (5.19%) 7 | 2 / 75 (2.67%) 2 | 2 / 59 (3.39%) 2 |
| Fatigue | | | |
| subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 4 / 75 (5.33%) 9 | 2 / 59 (3.39%) 3 |
| Injection site pruritus | | | |
| subjects affected / exposed occurrences (all) | 5 / 77 (6.49%) 38 | 0 / 75 (0.00%) 0 | 5 / 59 (8.47%) 61 |
| Injection site erythema | | | |
| subjects affected / exposed occurrences (all) | 6 / 77 (7.79%) 25 | 0 / 75 (0.00%) 0 | 6 / 59 (10.17%) 23 |
| Injection site reaction | | | |
| subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 3 | 0 / 75 (0.00%) 0 | 6 / 59 (10.17%) 13 |
| Gastrointestinal disorders | | | |
| Dyspepsia | | | |
| subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 4 / 75 (5.33%) 6 | 1 / 59 (1.69%) 2 |
| Eructation | | | |
| subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 4 | 5 / 75 (6.67%) 6 | 0 / 59 (0.00%) 0 |
| Diarrhoea | | | |
| subjects affected / exposed occurrences (all) | 10 / 77 (12.99%) 18 | 14 / 75 (18.67%) 21 | 5 / 59 (8.47%) 12 |
| Constipation | | | |
| subjects affected / exposed occurrences (all) | 6 / 77 (7.79%) 6 | 4 / 75 (5.33%) 6 | 3 / 59 (5.08%) 3 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 5 / 75 (6.67%) 6 | 0 / 59 (0.00%) 0 |
| Nausea | | | |

| | | | |
|--|------------------------|------------------------|---------------------|
| subjects affected / exposed occurrences (all) | 10 / 77 (12.99%) 13 | 17 / 75 (22.67%) 29 | 4 / 59 (6.78%) 8 |
| Vomiting subjects affected / exposed occurrences (all) | 5 / 77 (6.49%) 7 | 10 / 75 (13.33%) 12 | 2 / 59 (3.39%) 2 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 1 / 75 (1.33%) 1 | 1 / 59 (1.69%) 1 |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 9 / 77 (11.69%) 9 | 7 / 75 (9.33%) 7 | 2 / 59 (3.39%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 2 / 75 (2.67%) 2 | 4 / 59 (6.78%) 4 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 77 (2.60%) 2 | 3 / 75 (4.00%) 3 | 2 / 59 (3.39%) 2 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 7 / 77 (9.09%) 7 | 8 / 75 (10.67%) 8 | 0 / 59 (0.00%) 0 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 1 / 77 (1.30%) 1 | 0 / 75 (0.00%) 0 | 2 / 59 (3.39%) 2 |

| | | | |
|---|---------------------|--|--|
| Non-serious adverse events | Placebo | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 23 / 61 (37.70%) | | |
| Investigations Amylase increased subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | | |
| Lipase increased subjects affected / exposed occurrences (all) | 2 / 61 (3.28%) 2 | | |

| | | | |
|--|----------------|--|--|
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | | |
| occurrences (all) | 1 | | |
| Headache | | | |
| subjects affected / exposed | 2 / 61 (3.28%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | | |
| occurrences (all) | 1 | | |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eructation | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed occurrences (all)</p> <p>Constipation subjects affected / exposed occurrences (all)</p> <p>Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)</p> <p>Nausea subjects affected / exposed occurrences (all)</p> <p>Vomiting subjects affected / exposed occurrences (all)</p> | <p>7 / 61 (11.48%) 9</p> <p>1 / 61 (1.64%) 1</p> <p>1 / 61 (1.64%) 1</p> <p>1 / 61 (1.64%) 2</p> <p>1 / 61 (1.64%) 1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Back pain subjects affected / exposed occurrences (all)</p> | <p>2 / 61 (3.28%) 3</p> | | |
| <p>Infections and infestations</p> <p>COVID-19 subjects affected / exposed occurrences (all)</p> <p>Upper respiratory tract infection subjects affected / exposed occurrences (all)</p> <p>Nasopharyngitis subjects affected / exposed occurrences (all)</p> | <p>8 / 61 (13.11%) 8</p> <p>1 / 61 (1.64%) 1</p> <p>2 / 61 (3.28%) 2</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Decreased appetite subjects affected / exposed occurrences (all)</p> <p>Hyperglycaemia subjects affected / exposed occurrences (all)</p> | <p>1 / 61 (1.64%) 1</p> <p>6 / 61 (9.84%) 6</p> | | |

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