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 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 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 (± 18.4)	1.00 (± 28.2)	0.94 (± 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 (± 107.0)	0.54 (± 136.9)	0.64 (± 147.9)	0.66 (± 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 (± 141.5)	0.82 (± 89.7)	0.93 (± 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
VIth 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	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary fibrosis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Suicide attempt				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Humerus fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrioventricular block complete				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	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	1 / 77 (1.30%)	1 / 74 (1.35%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Injection site erythema			
subjects affected / exposed	0 / 77 (0.00%)	1 / 74 (1.35%)	4 / 77 (5.19%)
occurrences (all)	0	1	10
Injection site reaction			
subjects affected / exposed	1 / 77 (1.30%)	2 / 74 (2.70%)	2 / 77 (2.60%)
occurrences (all)	1	3	4
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	4 / 77 (5.19%)	3 / 74 (4.05%)	2 / 77 (2.60%)
occurrences (all)	4	4	2
Eructation			
subjects affected / exposed	1 / 77 (1.30%)	2 / 74 (2.70%)	1 / 77 (1.30%)
occurrences (all)	2	5	2
Diarrhoea			
subjects affected / exposed	11 / 77 (14.29%)	16 / 74 (21.62%)	11 / 77 (14.29%)
occurrences (all)	25	30	22
Constipation			
subjects affected / exposed	4 / 77 (5.19%)	6 / 74 (8.11%)	7 / 77 (9.09%)
occurrences (all)	4	7	7
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 77 (1.30%)	2 / 74 (2.70%)	2 / 77 (2.60%)
occurrences (all)	2	2	2
Nausea			
subjects affected / exposed	15 / 77 (19.48%)	9 / 74 (12.16%)	5 / 77 (6.49%)
occurrences (all)	21	25	8
Vomiting			
subjects affected / exposed	4 / 77 (5.19%)	7 / 74 (9.46%)	4 / 77 (5.19%)
occurrences (all)	4	9	4
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 77 (2.60%)	5 / 74 (6.76%)	3 / 77 (3.90%)
occurrences (all)	2	5	3
Infections and infestations			

COVID-19			
subjects affected / exposed	6 / 77 (7.79%)	4 / 74 (5.41%)	6 / 77 (7.79%)
occurrences (all)	7	4	6
Upper respiratory tract infection			
subjects affected / exposed	0 / 77 (0.00%)	2 / 74 (2.70%)	2 / 77 (2.60%)
occurrences (all)	0	2	2
Nasopharyngitis			
subjects affected / exposed	3 / 77 (3.90%)	4 / 74 (5.41%)	4 / 77 (5.19%)
occurrences (all)	4	4	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 77 (5.19%)	8 / 74 (10.81%)	3 / 77 (3.90%)
occurrences (all)	4	8	4
Hyperglycaemia			
subjects affected / exposed	1 / 77 (1.30%)	0 / 74 (0.00%)	2 / 77 (2.60%)
occurrences (all)	1	0	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	5 / 77 (6.49%)	1 / 75 (1.33%)	1 / 59 (1.69%)
occurrences (all)	5	1	1
Lipase increased			
subjects affected / exposed	7 / 77 (9.09%)	2 / 75 (2.67%)	1 / 59 (1.69%)
occurrences (all)	8	2	1
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 77 (3.90%)	5 / 75 (6.67%)	0 / 59 (0.00%)
occurrences (all)	4	6	0
Headache			

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

subjects affected / exposed	10 / 77 (12.99%)	17 / 75 (22.67%)	4 / 59 (6.78%)
occurrences (all)	13	29	8
Vomiting			
subjects affected / exposed	5 / 77 (6.49%)	10 / 75 (13.33%)	2 / 59 (3.39%)
occurrences (all)	7	12	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 77 (11.69%)	7 / 75 (9.33%)	2 / 59 (3.39%)
occurrences (all)	9	7	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 77 (2.60%)	2 / 75 (2.67%)	4 / 59 (6.78%)
occurrences (all)	2	2	4
Nasopharyngitis			
subjects affected / exposed	2 / 77 (2.60%)	3 / 75 (4.00%)	2 / 59 (3.39%)
occurrences (all)	2	3	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 77 (9.09%)	8 / 75 (10.67%)	0 / 59 (0.00%)
occurrences (all)	7	8	0
Hyperglycaemia			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	2 / 59 (3.39%)
occurrences (all)	1	0	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	0 / 61 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		

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

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

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