



Clinical trial results:

A 52 week study comparing the efficacy and safety of once weekly IcoSema and once weekly semaglutide, both treatment arms with or without oral anti diabetic drugs, in participants with type 2 diabetes inadequately controlled with a GLP 1 receptor agonist. COMBINE 2 Summary

EudraCT number	2020-005308-21
Trial protocol	SK GR SE HU
Global end of trial date	16 January 2024

Results information

Result version number	v1 (current)
This version publication date	01 February 2025
First version publication date	01 February 2025

Trial information

Trial identification

Sponsor protocol code	NN1535-4592
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05259033
WHO universal trial number (UTN)	U1111-1260-8268
Other trial identifiers	jRCT2051220044: Japanese trial registration number, CTR20220767: China Drug Trials (China)

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 March 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm superiority of once weekly IcoSema compared with once weekly semaglutide, both treatment arms with or without OADs, in terms of glycaemic control measured by change in HbA1c from baseline after 52 weeks in participants with T2D inadequately controlled with a GLP 1 receptor agonist.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki (64th World Medical Association [WMA] General Assembly, Fortaleza, Brazil. Oct 2013) and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	11 April 2022
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	Brazil: 63
Country: Number of subjects enrolled	Canada: 35
Country: Number of subjects enrolled	Switzerland: 13
Country: Number of subjects enrolled	China: 50
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Greece: 72
Country: Number of subjects enrolled	Hungary: 34
Country: Number of subjects enrolled	Israel: 35
Country: Number of subjects enrolled	Japan: 100
Country: Number of subjects enrolled	Slovakia: 46
Country: Number of subjects enrolled	Sweden: 9
Country: Number of subjects enrolled	Taiwan: 20
Country: Number of subjects enrolled	United States: 171
Worldwide total number of subjects	683
EEA total number of subjects	196

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)	455
From 65 to 84 years	228
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Trial was conducted at 124 sites in 13 countries as follows (number of sites that screened subjects/number of sites that randomised subjects): Brazil (6/6); Canada (10/9); China Mainland (11/11); France (5/5); Greece (8/8); Hungary (4/4); Israel (6/6); Japan (9/9); Slovakia (6/6); Sweden (3/3); Switzerland (3/3); Taiwan (5/5); United States (48/46).

Pre-assignment

Screening details:

Subjects were randomised in 1:1 ratio to receive subcutaneous (s.c.) injection of either IcoSema or semaglutide once weekly. The trial had a 52-week treatment 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	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	IcoSema

Arm description:

Subjects received once weekly 700 units per millilitre (U/mL) of insulin icodec and 2 milligram per millilitre (mg/mL) of semaglutide subcutaneously for 52 weeks. Participants were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose re-duced by 10 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 10 U. Dose titration of IcoSema was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Arm type	Experimental
Investigational medicinal product name	IcoSema
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received icodec once weekly subcutaneously.

Arm title	Semaglutide
------------------	-------------

Arm description:

Subjects received once weekly semaglutide subcutaneously in a dose escalation manner, with dose increases every 4 weeks for up to week 8 (0.25 milligrams [mg], 0.5 mg) followed by 1.0 mg once weekly up to the end of treatment period.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	Ozempic
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received semaglutide once weekly subcutaneously.

Number of subjects in period 1	IcoSema	Semaglutide
Started	342	341
Full analysis set (FAS)	342	341
Safety analysis set (SAS)	341	340
Exposed	341	340
Completed	329	336
Not completed	13	5
Consent withdrawn by subject	10	5
Death	2	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	IcoSema
Reporting group description:	
Subjects received once weekly 700 units per millilitre (U/mL) of insulin icodec and 2 milligram per millilitre (mg/mL) of semaglutide subcutaneously for 52 weeks. Participants were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose re-duced by 10 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 10 U. Dose titration of IcoSema was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.	
Reporting group title	Semaglutide
Reporting group description:	
Subjects received once weekly semaglutide subcutaneously in a dose escalation manner, with dose increases every 4 weeks for up to week 8 (0.25 milligrams [mg], 0.5 mg) followed by 1.0 mg once weekly up to the end of treatment period.	

Reporting group values	IcoSema	Semaglutide	Total
Number of subjects	342	341	683
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	213	242	455
From 65-84 years	129	99	228
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	59.9	58.3	
standard deviation	± 10.5	± 9.8	-
Sex: Female, Male			
Units: Participants			
Female	141	145	286
Male	201	196	397

End points

End points reporting groups

Reporting group title	IcoSema
-----------------------	---------

Reporting group description:

Subjects received once weekly 700 units per millilitre (U/mL) of insulin icodec and 2 milligram per millilitre (mg/mL) of semaglutide subcutaneously for 52 weeks. Participants were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 10 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 10 U. Dose titration of IcoSema was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Reporting group title	Semaglutide
-----------------------	-------------

Reporting group description:

Subjects received once weekly semaglutide subcutaneously in a dose escalation manner, with dose increases every 4 weeks for up to week 8 (0.25 milligrams [mg], 0.5 mg) followed by 1.0 mg once weekly up to the end of treatment period.

Primary: Change in glycosylated haemoglobin (HbA1c)

End point title	Change in glycosylated haemoglobin (HbA1c)
-----------------	--

End point description:

Change from baseline (week 0) to week 52 in HbA1c is presented. The outcome measure was evaluated based on the data from in study period, where all data from randomisation until last date of any of the following: 1) last direct subjects-site contact; 2) subjects who withdrew their informed consent; 3) last subjects-investigator contact as defined by the investigator for subjects who lost to follow-up (i.e. possibly an unscheduled phone visit); 4) death of subjects who died before any of the above. Full Analysis Set (FAS) which comprised all randomised subjects. Number of subjects analyzed = subjects with available data for this outcome measure.

End point type	Primary
----------------	---------

End point timeframe:

From baseline week 0 (V2) to week 52 (V54)

End point values	IcoSema	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	335		
Units: Percentage point of HbA1c				
arithmetic mean (standard deviation)	-1.40 (± 0.91)	-0.86 (± 0.96)		

Statistical analyses

Statistical analysis title	IcoSema - Semaglutide
----------------------------	-----------------------

Statistical analysis description:

Hypothetical estimand

Comparison groups	IcoSema v Semaglutide
-------------------	-----------------------

Number of subjects included in analysis	660
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Estimated treatment difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	-0.33

Secondary: Change in fasting plasma glucose (FPG)

End point title	Change in fasting plasma glucose (FPG)
End point description:	
Change from baseline (week 0) to week 52 in FPG is presented. The outcome measure was evaluated based on the data from in study period, where all data from randomisation until last date of any of the following: 1) last direct subjects-site contact; 2) subjects who withdrew their informed consent; 3) last subjects-investigator contact as defined by the investigator for subjects who lost to follow-up (i.e. possibly an unscheduled phone visit); 4) death of subjects who died before any of the above. FAS which comprised all randomised subjects. Number of subjects analyzed = subjects with available data for this outcome measure.	
End point type	Secondary
End point timeframe:	
From baseline week 0 (V2) to week 52 (V54)	

End point values	IcoSema	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	317		
Units: Millimoles per litre (mmol/L)				
arithmetic mean (standard deviation)	-2.74 (± 2.85)	-1.41 (± 2.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter)
End point description:	
Hypoglycaemic episodes were classified according to the American Diabetes Association/ International Hypoglycaemia Study Group, where glycemic criteria for level 2 was < 3.0 mmol/L (54 mg/dL). The outcome measure was evaluated based on data from on treatment period, where all data from date of first dose of randomised treatment as recorded on the electronic case report form (eCRF) until the first date of any of the following: 1) last follow-up visit (V56); 2) last date on randomised treatment +6	

weeks (corresponding to 5 weeks after the end of the dosing interval for both treatment arms); 3) end-date for the in-study data points sets. SAS included all subjects exposed to randomised treatment.

End point type	Secondary
End point timeframe:	
From baseline week 0 (V2) to week 57 (V56)	

End point values	IcoSema	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	341	340		
Units: Episodes				
number (not applicable)	15	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L [54 mg/dL], confirmed by blood glucose [BG] meter) or severe hypoglycaemic episodes (level 3)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L [54 mg/dL], confirmed by blood glucose [BG] meter) or severe hypoglycaemic episodes (level 3)
-----------------	--

End point description:

Hypoglycaemic episodes were classified according to the American Diabetes Association/ International Hypoglycaemia Study Group, where glycemic criteria for level 2 was less than (<) 3.0 mmol/L (54 milligram per decilitre [mg/dL]) and level 3 had no specific glucose threshold. The outcome measure was evaluated based on data from on treatment period, where all data from date of first dose of randomised treatment as recorded on the electronic case report form (eCRF) until the first date of any of the following: 1) last follow-up visit (V56); 2) last date on randomised treatment +6 weeks (corresponding to 5 weeks after the end of the dosing interval for both treatment arms); 3) end-date for the in-study data points sets. Safety Analysis Set (SAS) included all subjects exposed to randomised treatment.

End point type	Secondary
End point timeframe:	
From baseline week 0 (V2) to week 57 (V56)	

End point values	IcoSema	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	341	340		
Units: Episodes				
number (not applicable)	15	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of severe hypoglycaemic episodes (level 3)

End point title	Number of severe hypoglycaemic episodes (level 3)
-----------------	---

End point description:

Hypoglycaemic episodes were classified according to the American Diabetes Association/ International Hypoglycaemia Study Group, where glycemic criteria for level 3 had no specific glucose threshold. The outcome measure was evaluated based on data from on treatment period, where all data from date of first dose of randomised treatment as recorded on the electronic case report form (eCRF) until the first date of any of the following: 1) last follow-up visit (V56); 2) last date on randomised treatment +6 weeks (corresponding to 5 weeks after the end of the dosing interval for both treatment arms); 3) end-date for the in-study data points sets. SAS included all subjects exposed to randomised treatment.

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

End point timeframe:

From baseline week 0 (V2) to week 57 (V56)

End point values	IcoSema	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	341	340		
Units: Episodes				
number (not applicable)	0	0		

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 (week 0) to week 52 in body weight is presented. The outcome measure was evaluated based on the data from in study period, where all data from randomisation until last date of any of the following: 1) last direct subjects-site contact; 2) subjects who withdrew their informed consent; 3) last subjects-investigator contact as defined by the investigator for subjects who lost to follow-up (i.e. possibly an unscheduled phone visit); 4) death of subjects who died before any of the above. FAS which comprised all randomised subjects. Number of subjects analyzed = subjects with available data for this outcome measure.

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

End point timeframe:

From baseline week 0 (V2) to week 52 (V54)

End point values	IcoSema	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	336		
Units: Kilogram (kg)				
arithmetic mean (standard deviation)	0.89 (± 4.36)	-3.77 (± 4.60)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 0 to week 57.

Adverse event reporting additional description:

Presented AEs are TEAEs, defined as event with onset during on treatment period. Results are based on SAS including all subjects exposed to randomised treatment.

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

Dictionary used

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

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

Reporting groups

Reporting group title	Semaglutide
-----------------------	-------------

Reporting group description:

Subjects received once weekly semaglutide subcutaneously in a dose escalation manner, with dose increases every 4 weeks for up to week 8 (0.25 milligrams [mg], 0.5 mg) followed by 1.0 mg once weekly up to the end of treatment period.

Reporting group title	IcoSema
-----------------------	---------

Reporting group description:

Subjects received once weekly 700 units per millilitre (U/mL) of insulin icodec and 2 milligram per millilitre (mg/mL) of semaglutide subcutaneously for 52 weeks. Participants were to perform once daily pre-breakfast self-monitoring plasma glucose (SMPG). The dose was adjusted based on 3 pre-breakfast SMPG values measured on the 2 previous days and the day of the contact. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose re-duced by 10 U; 4.4-7.2 mmol/L: no adjustment; > 7.2 mmol/L: dose increased by 10 U. Dose titration of IcoSema was based on the respective premeal(s) and bedtime self-measured plasma glucose (SMPG) measured weekly.

Serious adverse events	Semaglutide	IcoSema	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 340 (6.18%)	38 / 341 (11.14%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acoustic neuroma			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenoma			

subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of head and neck			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Cardioversion			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Femoral neck fracture			
subjects affected / exposed	1 / 340 (0.29%)	3 / 341 (0.88%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Angina unstable			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 340 (0.00%)	2 / 341 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 340 (0.00%)	2 / 341 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral infarction			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine without aura			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIth nerve paralysis			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Cataract			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colon dysplasia			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 340 (0.29%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 340 (0.29%)	2 / 341 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 340 (0.29%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 340 (0.00%)	2 / 341 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	2 / 340 (0.59%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal sepsis			

subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media chronic			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 340 (0.29%)	2 / 341 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 340 (0.00%)	1 / 341 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			

subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 340 (0.29%)	0 / 341 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Semaglutide	IcoSema	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 340 (46.76%)	163 / 341 (47.80%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 340 (1.76%)	20 / 341 (5.87%)	
occurrences (all)	6	25	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	10 / 340 (2.94%)	19 / 341 (5.57%)	
occurrences (all)	10	20	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	17 / 340 (5.00%)	11 / 341 (3.23%)	
occurrences (all)	22	14	
Diarrhoea			
subjects affected / exposed	41 / 340 (12.06%)	38 / 341 (11.14%)	
occurrences (all)	82	53	
Vomiting			
subjects affected / exposed	22 / 340 (6.47%)	17 / 341 (4.99%)	
occurrences (all)	48	24	
Nausea			

subjects affected / exposed occurrences (all)	39 / 340 (11.47%) 73	40 / 341 (11.73%) 65	
Infections and infestations			
COVID-19			
subjects affected / exposed	49 / 340 (14.41%)	51 / 341 (14.96%)	
occurrences (all)	53	52	
Nasopharyngitis			
subjects affected / exposed	33 / 340 (9.71%)	33 / 341 (9.68%)	
occurrences (all)	45	45	
Upper respiratory tract infection			
subjects affected / exposed	29 / 340 (8.53%)	22 / 341 (6.45%)	
occurrences (all)	34	34	

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