Clinical trial results:
Semaglutide as an adjunct to dieting in the treatment of type 2 diabetes – effects on glucose metabolism, prevention of weight regain and peripheral tissue metabolic activation

Summary

EudraCT number	2020-002712-51
Trial protocol	FI
Global end of trial date	18 December 2024

Results information

Result version number	v1 (current)
This version publication date	05 June 2026
First version publication date	05 June 2026

Trial information

Trial identification

Sponsor protocol code	2020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04854083
WHO universal trial number (UTN)	U1111-1257-6747

Notes:

Sponsors

Sponsor organisation name	Kirsi Pietiläinen, University of Helsinki
Sponsor organisation address	Haartmaninkatu 8, Helsinki, Finland, 00290
Public contact	Lihavuustutkimusyksikkö, Obesity Research Unit / Lihavuustutkimusyksikkö, lihavuustutkimusyksikko@gmail.com
Scientific contact	Lihavuustutkimusyksikkö, Obesity Research Unit / Lihavuustutkimusyksikkö, +358 505992295, lihavuustutkimusyksikko@gmail.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	23 March 2026
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2024
Global end of trial reached?	Yes
Global end of trial date	18 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the effect of subcutaneous 1mg once weekly semaglutide treatment compared with placebo treatment on glucose homeostasis (HbA1c) in patients with T2DM following diet-induced weight loss intervention at 12 months.

Protection of trial subjects:

The safety and tolerability of the study procedures were assessed throughout the trial, for example by monitoring adverse events, laboratory parameters, vital signs, and findings from physical examinations. Any adverse effects were treated as needed during the study. Participants in both groups could experience discomfort or adverse effects related to injections, tissue sampling, and laboratory tests. However, all procedures employed have been routinely performed at our study site for several years, and the experienced study staff consistently prioritised safety and reliability.
The weight-loss intervention could also cause discomfort, such as constipation, headache, and fatigue. The intervention was implemented with particular care to minimise the risk of muscle loss or micronutrient deficiencies, and nutritional status was evaluated and counselling provided at each study visit by a registered dietitian. To ensure participant safety and to prevent misunderstandings regarding any aspect of the study procedures, only Finnish-speaking participants were recruited, in accordance with the study protocol. In the event of an emergency, the study blind could be broken at the investigator’s discretion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 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	Finland: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment targeted T2DM clinics and advertisements were shared via hospital and university websites. Interested patients received a study info by email, then completed phone pre-screening and screening scheduling. Recruitment lasted up to 18 months.

Pre-assignment

Screening details:

Inclusion criteria were age ≥18 years and <65 years , BMI ≥27 kg/m2 and T2DM (HbA1c 6.0% if on anti-diabetic medication or HbA1c 6.5% if non-medicated). In total, 26 individuals attended the eligibility assessment visit, of whom 20 met the inclusion criteria and were willing and able to give informed consent for participation in the study.

Period 1

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

Blinding implementation details:

At the 8-week time point after the low calorie diet phase, the patients were randomized in a 1:1 manner to either semaglutide or placebo. The randomization was done so that semaglutide and placebo groups had similar shares of sexes and similar mean age, and BMI. The study blind could have been broken in a case of emergency by the judgement of the investigator, but there was no need for that.

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide

Arm description:

The intervention study for the patients with T2DM began with a low-calorie diet (LCD) phase run-in for 13 weeks for all subjects including 8 weeks of total LCD followed 5-week gradual re-introduction of food (replacement of the VLCD products by one meal/week). During re-introduction of food, the subjects were randomly assigned to semaglutide or placebo (subcutaneous administration, dose escalation 0.25 mg once weekly for 4 weeks, 0.5 mg once weekly for 4 weeks, where after 1.0 mg once weekly) until the end of the study (12 months).

Arm type	Experimental
Investigational medicinal product name	semaglutide
Investigational medicinal product code	
Other name	Ozempic®
Pharmaceutical forms	Suspension for injection in pre-filled injector
Routes of administration	Subcutaneous use

Dosage and administration details:

The investigational product used in the trial was semaglutide 1 mg/week or placebo, formulated as a solution for subcutaneous injection in a pre-filled pen injector. Semaglutide and placebo were visually identical and packaged in a blinded manner to maintain double-blind treatment conditions. All participants were instructed on how to self-administer the weekly injections. Dose escalation was carried out in two titration steps, beginning with 0.25 mg once weekly for 4 weeks, followed by 0.5 mg once weekly for a further 4 weeks, after which 1.0 mg was administered once weekly until the end of the 12-month study period.

Arm title	Placebo

Arm description:

We compared the effects of semaglutide 1 mg weekly vs. normal dieting by randomizing the patients with both T2DM and overweight/obesity (BMI≥27) (n=20, aged ≥18 to < 65 years) to two groups: both groups participated in a similar lifestyle treatment to induce weight loss, but one group got an add-on of semaglutide 1.34mg/ml while the other was treated with placebo.

Arm type	Placebo

Investigational medicinal product name	semaglutide
Investigational medicinal product code	
Other name	Ozempic
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

The subjects self-administered semaglutide (1.34 mg/mL) or placebo once weekly at home after receiving training on the correct subcutaneous injection technique. Dosing was escalated from 0.25 mg once weekly for 4 weeks to 0.5 mg once weekly for 4 weeks, followed by 1.0 mg once weekly until the end of the 12-month study.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

The subjects self-administered semaglutide (1.34 mg/mL) or placebo once weekly at home after receiving training on the correct subcutaneous injection technique. Dosing was escalated from 0.25 mg once weekly for 4 weeks to 0.5 mg once weekly for 4 weeks, followed by 1.0 mg once weekly until the end of the 12-month study.

Number of subjects in period 1	Semaglutide	Placebo
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide

Reporting group description:

The intervention study for the patients with T2DM began with a low-calorie diet (LCD) phase run-in for 13 weeks for all subjects including 8 weeks of total LCD followed 5-week gradual re-introduction of food (replacement of the VLCD products by one meal/week). During re-introduction of food, the subjects were randomly assigned to semaglutide or placebo (subcutaneous administration, dose escalation 0.25 mg once weekly for 4 weeks, 0.5 mg once weekly for 4 weeks, where after 1.0 mg once weekly) until the end of the study (12 months).

Reporting group title	Placebo

Reporting group description:

We compared the effects of semaglutide 1 mg weekly vs. normal dieting by randomizing the patients with both T2DM and overweight/obesity (BMI≥27) (n=20, aged ≥18 to < 65 years) to two groups: both groups participated in a similar lifestyle treatment to induce weight loss, but one group got an add-on of semaglutide 1.34mg/ml while the other was treated with placebo.

Reporting group values	Semaglutide	Placebo	Total
Number of subjects	10	10	20
Age categorical			
The mean (SD) age was 53.0 (9.3) years in the semaglutide group and 52.3 (6.7) years in the placebo group.			
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)	10	10	20
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	53.0	52.3	
standard deviation	± 9.3	± 6.7	-
Gender categorical			
Units: Subjects			
Female	9	9	18
Male	1	1	2

End points

End points reporting groups

Reporting group title	Semaglutide

Reporting group description:

The intervention study for the patients with T2DM began with a low-calorie diet (LCD) phase run-in for 13 weeks for all subjects including 8 weeks of total LCD followed 5-week gradual re-introduction of food (replacement of the VLCD products by one meal/week). During re-introduction of food, the subjects were randomly assigned to semaglutide or placebo (subcutaneous administration, dose escalation 0.25 mg once weekly for 4 weeks, 0.5 mg once weekly for 4 weeks, where after 1.0 mg once weekly) until the end of the study (12 months).

Reporting group title	Placebo

Reporting group description:

We compared the effects of semaglutide 1 mg weekly vs. normal dieting by randomizing the patients with both T2DM and overweight/obesity (BMI≥27) (n=20, aged ≥18 to < 65 years) to two groups: both groups participated in a similar lifestyle treatment to induce weight loss, but one group got an add-on of semaglutide 1.34mg/ml while the other was treated with placebo.

Primary: Change in HbA1c

End point title	Change in HbA1c

End point description:

End point type	Primary

End point timeframe:

From baseline to 12 months

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/mol				
arithmetic mean (confidence interval 95%)	-13.3 (-15.1 to -10.8)	-8.4 (-10.9 to -6.0)		

Statistical analyses

Statistical analysis title	Linear mixed-effects regression modeling

Statistical analysis description:

We estimated treatment effects at each timepoint using linear mixed effects model (R package lme4). Models included mean-centered baseline values as a fixed-effect covariate, and participant ID as a random-effect covariate. For each outcome, we used an interaction model to evaluate the effect of the semaglutide treatment, i.e. the estimated treatment difference.

Comparison groups	Semaglutide v Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.01
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	-1.2

Notes:

[1] - Mixed models analysis

Secondary: Body weight change

End point title	Body weight change

End point description:

End point type	Secondary

End point timeframe:

From baseline to 12 months

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: kilogram(s)				
arithmetic mean (confidence interval 95%)	-15.3 (-19.4 to -11.1)	-7.1 (-11.2 to -3.0)		

Statistical analyses

Statistical analysis title	Linear mixed-effects regression modeling

Statistical analysis description:

We estimated treatment effects at each timepoint using linear mixed effects model (R package lme4). Models included mean-centered baseline values as a fixed-effect covariate, and participant ID as a random-effect covariate. For each outcome, we used an interaction model to evaluate the effect of the semaglutide treatment, i.e. the estimated treatment difference.

Comparison groups	Semaglutide v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.008
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-8.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.1
upper limit	-2.3

Adverse events

Adverse events information

Timeframe for reporting adverse events:

We recruited the first participant on February 16, 2022, and the last study visit conducted on December 18, 2024 and between these time point all adverse events were reported.

Adverse event reporting additional description:

Adverse events were reported in both treatment groups and were predominantly mild to moderate in severity. The types of events observed were broadly similar between groups.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28

Reporting groups

Reporting group title	Semaglutide

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Semaglutide	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Semaglutide	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 10 (100.00%)	
Cardiac disorders			
Hypertension			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Angina pectoris			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Arrhythmia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Migraine			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	4 / 10 (40.00%)	
occurrences (all)	1	4	
Vertigo positional	Additional description: Benign paroxysmal positional vertigo		
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Injection site reaction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sweating			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 10 (90.00%)	5 / 10 (50.00%)	
occurrences (all)	11	5	
Diarrhoea			
subjects affected / exposed	4 / 10 (40.00%)	4 / 10 (40.00%)	
occurrences (all)	12	4	
Constipation			
subjects affected / exposed	3 / 10 (30.00%)	4 / 10 (40.00%)	
occurrences (all)	6	5	
Flatulence			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	
occurrences (all)	2	3	
Vomiting			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	
occurrences (all)	1	3	
Hernia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eructation			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Decreased appetite			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psoriasis aggravated			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rosacea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Knee pain			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Arthralgia	Additional description: Arthralgia / leg pain (biopsy site pain)		
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Rotator cuff injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pain in extremity	Additional description: Pain in extremity (right leg)		
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Infections and infestations			
Influenza			
subjects affected / exposed	6 / 10 (60.00%)	7 / 10 (70.00%)	
occurrences (all)	10	12	
COVID-19			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	
occurrences (all)	3	3	
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Gastroenteritis			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Pharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Eye infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

Metabolism and nutrition disorders Blood glucose increased subjects affected / exposed occurrences (all)	 0 / 10 (0.00%) 0	 1 / 10 (10.00%) 1	

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