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A trial of 26 weeks of subcutaneous liraglutide (a GLP1 receptor agonist), with or without continuous positive airway pressure (CPAP), in patients with type 2 diabetes mellitus (T2DM) and obstructive sleep apnoea (OSA)

Submission date 19/08/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 19/08/2015	**Overall study status** Completed	
Last Edited 11/12/2020	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Obstructive sleep apnoea (OSA) is a condition where there is repeated closing of the upper airway during sleep. It can cause snoring, waking during sleep and periods of not being able to breathe. People who are obese with type 2 diabetes mellitus (T2DM) are at particularly high risk of developing OSA; approximately 86% have the condition. If not given effective treatment OSA can lead to long-term health issues. Current treatment options for OSA include losing weight (via either a very low energy diet, intensive lifestyle changes or metabolic surgery) or, in the absence of weight loss, a continuous positive airway pressure (CPAP) device that prevent the airway closing while the patient is asleep. However, compliance with these treatments is poor. Glucagon-like peptide receptor agonist (GLP1-RA) therapy is commonly used in the treatment of diabetes. This drug has been shown to improve obesity and insulin resistance. To date, there have been no studies to examine the effects of GLP1-RA on OSA in patients with T2DM. This study will examine the effectiveness of 26 weeks of GLP1-RA, with and without CPAP, in obese patients with OSA and T2DM.

Who can participate?
Adults aged 18-75 with OSA and T2DM

What does the study involve?
Patients first have a series of physiological assessments to examine metabolic and cardiovascular (for example heart) health. They are then randomly allocated into one of 4 groups and treated accordingly: control (no treatment), GLP1-RA, CPAP, and finally GLP1-RA and CPAP. All assessments are repeated after the study period of 26 weeks.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
GP and out-patients clinics across the Liverpool and Newcastle areas (UK)

When is the study starting and how long is it expected to run for?
September 2015 to October 2019

Who is funding the study?
Novo Nordisk UK Research Foundation

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19540

Study information

Scientific Title
A randomised, controlled multi-centre trial of 26 weeks of subcutaneous liraglutide (a GLP1 receptor agonist), with or without continuous positive airway pressure (CPAP), in patients with type 2 diabetes mellitus (T2DM) and obstructive sleep apnoea (OSA)

Acronym
ROMANCE

Study objectives
The aim of this study is to examine the efficacy of 26- weeks of glucagon--like peptide receptor agonist (GLP1-RA) therapy , with and without continuous positive airway pressure (CPAP) treatment in obese patients with obstructive sleep apnoea (OSA) and type 2 diabetes mellitus (T2DM).

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/NW/1019

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Diabetes, sleep apnoea

Interventions
Following screening, patients with OSA and T2DM will be recruited from primary (GPs) and secondary care settings (out-patients clinics) across the Liverpool and Newcastle areas. After informed consent has been obtained patients will undergo a series of physiological assessments to examine metabolic and cardiovascular health and will then randomised to one of the following interventions:
1. Control (no intervention)
2. GLP1-RA
3. CPAP
4. GLP1-RA & CPAP
All assessments will be repeated following the intervention period.

Intervention Type

Drug

Phase
Phase III/IV

Drug/device/biological/vaccine name(s)
Liraglutide

Primary outcome measure
Liraglutide treatment

Secondary outcome measures
N/A

Overall study start date
01/09/2015

Completion date
10/10/2019

Eligibility

Key inclusion criteria
1. Males or females, age 18--75 years
2. Reproductive Status: Definition of Women of Child -Bearing Potential (WOCBP). WOCBP comprises women who have experienced menarche and who have not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or who are not post-menopausal (see definition below)
3. WOCBP must have a negative serum or urine pregnancy test result (minimum sensitivity 25 IU /L or equivalent units of HCG) within 0 to 72 hours before the first dose of study drug.
4. A clinical diagnosis of type 2 diabetes
5. Glycosylated haemoglobin (HbA1c) >53mmol/mol
6. BMI>30kg/ m2
7. Currently treated with either diet or any combination of metformin and sulphonylureas (excluding patients treated with DPP-IV inhibitors*, pioglitazone or insulin)
8. No current use of Liraglutide treatment
9. Patients with moderate-severe OSA as assessed by polysomnographic criteria, either by:
9.1. Apnoea-hypopnea index (AHI) >15 events/hour) with overnight domiciliary multichannel sleep study (ResMed, Apnoea Link™ or other suitable alternative)
9.2. Overnight desaturation index (pulse oximetry): ODI>10 (4% dip in oxygen saturation more than 10 events/hour)
9.3. Currently symptomatic for OSA, with excessive daytime sleepiness

*Patients who are currently treated with DPP-IV inhibitors can be included providing the treatment is discontinued before baseline tests.

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 152; UK Sample Size: 152

Key exclusion criteria
1. Medical History and Concurrent Diseases
2. Females of childbearing age who are not using adequate contraceptive methods or who are planning a pregnancy in the next 6 months
3. Treatment with DPP-IV inhibitors, pioglitazone or subcutaneous insulin injections or with the anti-obesity medication, orlistat
4. Patients in whom there may be occupational implications to a diagnosis of OSA e.g. professional drivers or operating machinery
5. Type 1 diabetes mellitus
6. Congestive heart failure class III-IV
7. Renal impairment: eGFR less than 30 ml/minute/1.73m2
8. Previous history of acute pancreatitis
9. Hyperthyroidism
10. Hypothyroidism (subjects with a normal TSH and free T4, and on a stable dose of thyroxine for at least 3 months may be included)
11. Uncontrolled hypertension (blood pressure >170/120 mmHg)
12. Recent (< 6 months) myocardial infarction
13. Previous stroke (with residual neurological deficit)
14. Significant cardiac dysrhythmias (including pacemaker or ICD)
15. Presence of any other medical condition that would, in the opinion of the investigator or their clinician preclude safe participation in the study. This decision should be informed by Liraglutide precautions for use statements which will be provided to all clinicians and the research team
16. Alcohol consumption in excess of daily recommended limits (21 units/week females, 28 units /week males)
17. Any history of internal metal, pacemakers, or ferromagnetic metallic implants intraocular foreign bodies or cerebral aneurysm clips (exclusion from MR scanning)
18. History of seizures or unexplained syncope
19. Severe sleepiness
20. Weight <140kg (due to limitations of MRI scanner)
21. Subjects with a history of any serious hypersensitivity reaction to GLP1-RA
22. WOCBP who are unwilling or unable to use an acceptable method to avoid pregnancy for the study duration plus 8 weeks after the last dose of study drug in such a manner that the risk of pregnancy is minimized
23. Women who are pregnant or breastfeeding
24. Diabetes treated with pioglitazone, GLP-1 analogues or insulin
25. Use of other weight loss medication or any drug that might affect body weight or appetite (including anti-depressants, antipsychotics, corticosteroids)

26. Prisoners or subjects who are involuntarily incarcerated
27. Subjects who are compulsorily detained for treatment of either a psychiatric or physical (e.g., infectious disease) illness

Date of first enrolment
01/09/2015

Date of final enrolment
01/10/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cancer Research UK
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Sponsor type
University/education

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ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Charity

Funder Name
Novo Nordisk UK Research Foundation

Alternative Name(s)
The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	22/07/2020	11/12/2020	Yes	No
HRA research summary			26/07/2023	No	No