

# The effects of liraglutide in controlling blood sugar and weight in poor-responders to bariatric surgery

<b>Submission date</b> 20/01/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 20/01/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 30/07/2019	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Type 2 diabetes mellitus (T2DM) is a growing problem worldwide. People with T2DM have difficulty controlling their blood sugar (glucose) as they do not produce enough insulin to function properly (insulin deficiency), or that the body's cells don't react to insulin as they should do (insulin resistance). One of the main reasons why people develop T2DM is because they are overweight or obese. Weight loss surgery, also called bariatric surgery, is a drastic measure used to help people who are dangerously overweight. There are a number of different types of bariatric surgery; however they all work by limiting the amount a person can eat or reducing the number of calories that are absorbed from food. In some patients, bariatric surgery can cause up to 30% weight loss and substantially improve blood glucose control however this is not always the case. Studies have shown that in patients where the procedures are successful, high amounts of a hormone called glucagon like peptide-1 or GLP-1 are produced. This hormone is responsible for causing insulin to be released, which reduces blood sugar. Liraglutide is a drug which has been developed to mimic the action of GLP-1. In the past, it has been given to overweight diabetics who aren't suitable for bariatric surgery, and has been found to lower blood glucose and weight. The aim of this study is to look at the effects of receiving liraglutide injections on blood glucose and weight in diabetic adults who have not responded well to bariatric surgery.

### Who can participate?

Adults with T2DM who have had a bariatric surgery 12 months ago.

### What does the study involve?

For the first two weeks of the study, all participants are taught how to use the injector pen device and asked to inject themselves with a dummy (placebo) every day. At the end of the two weeks, the devices are measured in order to find out how well each participant stuck to the regime. Participants are then randomly allocated to one of two groups. Participants in the first group are given pens containing liraglutide to use every day. For one week, a dose of 0.6mg/day is taken, then 1.2mg/day for the next week and then 1.8mg/day for the following week. After this, participants are given the opportunity to adjust the dose if they are experiencing a lot of

side effects. Participants in the second group are given pens containing a dummy (placebo) to use every day at the same doses as the first group. At the start of the study and then again after 26 weeks, participants in both groups attend follow up appointments so that their weight and blood sugar levels (in a blood test) can be measured.

What are the possible benefits and risks of participating?

Participants in both groups will benefit from being under the care of a specialist team which they would not normally have access to. The patients taking the liraglutide may also benefit from improvements to their diabetes management and weight loss. There is a risk of pain and discomfort from the injections, as well as when blood is taken to test blood sugar levels. There is also a risk of side effects from the liraglutide, however these will be closely monitored.

Where is the study run from?

Imperial College London (UK)

When is the study starting and how long is it expected to run for?

April 2015 to October 2017

Who is funding the study?

J P Moulton Charitable Foundation (UK)

Who is the main contact?

1. Dr Belen Perez Pevida

2. Dr Alex Miras

## Contact information

### Type(s)

Scientific

### Contact name

Dr Alex Miras

### Contact details

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## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

2014-003923-23

### **Protocol serial number**

20510

## **Study information**

### **Scientific Title**

The GRAVITAS trial: GLP-1 Receptor Agonist interVentlon for poor responders afTer bariAtric Surgery

### **Acronym**

GRAVITAS

### **Study objectives**

The aim of this study is to investigate whether daily injections of GLP-1 helps to reduce blood glucose and weight in bariatric surgery patients.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

West London & GTAC Research Ethics Committee, 21/11/2015, ref: 15/LO/0780

### **Study design**

Randomised; Interventional; Design type: Treatment

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Topic: Diabetes, Metabolic and endocrine disorders; Subtopic: Type 2, Metabolic and Endocrine (all Subtopics); Disease: Diabetic Control, Metabolic & Endocrine (not diabetes)

### **Interventions**

For the the two weeks of the run-in period (Trial Weeks 0-2), patients will be instructed on how to use the pen devices and self-administer placebo once a day. At the end of the run-in period, the pen devices will be collected and the remaining volume measured to check for patient adherence to the self-administration regime.

Participants are then randomly allocated to the intervention group or the control group in a 2:1 ratio.

**Intervention group:** Participants are asked to self-administer subcutaneous daily injections of liraglutide. The starting dose will be 0.6 mg/day for one week (trial week 2), 1.2 mg/day for the next week (trial week 3), and then 1.8 mg/day for the next week (trial week 4). During Trial Weeks 5-6, an assessment will be made of adverse effects, and if necessary the dose can be reduced. From Trial Week 6 onwards, participants will take their maximum tolerated dose (0.6 mg/day, 1.2 mg/day, or 1.8 mg/day).

**Control group:** Participants are asked to self-administer subcutaneous daily injections of saline (placebo) at the same doses as the intervention group.

The clinical research team will provide patients with a capillary glucose meter, inform them of possible side effects of liraglutide (e.g. nausea, vomiting, constipation or diarrhoea, hypoglycaemia and possible dehydration), and advise them as to how to deal with them. Patients will also be informed of the rare complication of pancreatitis and will be specifically instructed to urgently report any symptoms of abdominal pain to the clinical research team.

## **Intervention Type**

Other

## **Primary outcome(s)**

Diabetes management is assessed by measuring glycated hemoglobin (HbA1C) at baseline and 26 weeks.

## **Key secondary outcome(s)**

1. Body weight is measured using scales at baseline and 26 weeks
2. Blood pressure is measured using a sphygmomanometer at baseline and 26 weeks
3. Total number of medications taken by participants is measured by self-reporting at baseline and 26 weeks
4. Insulin dose for those patients taking insulin as treatment for T2DM is measured by self-reporting at baseline and 26 weeks
5. Obesity-related comorbidities are assessed using the King's obesity staging system at baseline and 26 weeks
6. Quality of life measured using the following questionnaires at baseline and 26 weeks:
  - 6.1. Dutch Eating Behaviour Questionnaire (DEBQ)
  - 6.2. Eating Disorder Examination Questionnaire (EDE-Q)
  - 6.3. Eating Attitudes Test (EAT)
  - 6.4. Behavioural Inhibition and Activation System (BIS / BAS) scales
  - 6.5. Eysenck Personality Questionnaire (EPQ-R)
  - 6.6. Beck Depression Inventory (BDI-II)
  - 6.7. Barratt Impulsivity Scale
  - 6.8. Three Factor Eating Questionnaire (TFEQ)
  - 6.9. Positive and Negative Affect Schedule (PANAS)
  - 6.10. Yale Food Addiction Scale, Power of Food questionnaire
  - 6.11. Alcohol Use Disorders Identification Test
7. Total caloric intake and macronutrient composition is measured using food diaries at baseline and 26 weeks
8. Food related behavioral traits (e.g. ad libitum total food intake, sweet taste detection threshold, consummatory taste reward ratings, and wanting and liking for food pictures) are assessed using dietary recall, sweet taste detection testing, consummatory taste reward test and

a computer task (to assess liking and wanting for different food pictures) at baseline and 26 weeks

9. Number of hypoglycaemic episodes experienced by participants is measured by self-reporting at baseline and 26 weeks

**Completion date**

01/02/2019

## **Eligibility**

**Key inclusion criteria**

1. Aged between 18- and 70 years
2. 12 months after gastric bypass or sleeve gastrectomy bariatric surgery
3. Diagnosed with Type 2 diabetes mellitus
4. HbA1c greater than 6.5% (more than 48 mmol/mol) on screening
5. On Metformin ± long acting insulin
6. Able to give informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

80

**Key exclusion criteria**

1. Diagnosis of Type 1 diabetes mellitus
2. Anatomical or endocrinological pathology causing poor weight loss or weight regain
3. Screening calcitonin of 50 ng/L or above
4. Family or personal history of multiple endocrine neoplasia type 2 or familial medullary thyroid carcinoma
5. Personal history of non-familial medullary thyroid carcinoma
6. History of acute or chronic pancreatitis
7. Uncontrolled hypertension (systolic blood pressure of 160 mmHg or above and/or diastolic blood pressure of 100 mmHg or above)
8. Estimated glomerular filtration rate (eGFR) less than 30 ml/min per 1.73 m<sup>2</sup>
9. Current pregnancy
10. Inability to maintain adequate contraception

**Date of first enrolment**

22/01/2016

**Date of final enrolment**

21/07/2017

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre****Imperial College London**

Du Cane Road

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## Sponsor information

**Organisation**

Imperial College London

**ROR**

<https://ror.org/041kmwe10>

## Funder(s)

**Funder type**

Charity

**Funder Name**

J P Moulton Charitable Foundation

## Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Belen Perez Pevida or Dr Alex Miras.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/07/2019	10/06/2019	Yes	No
<a href="#">Basic results</a>		30/07/2019	30/07/2019	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No