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Testing the safety and effects of a new drug (G3215) in adult subjects

Submission date	Recruitment status	[_] Prospectively registered
23/10/2020	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
03/11/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
18/01/2024	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol

Background and study aims
Obesity (defined as a BMI of more than 30 kg/m2) reduces life expectancy and increases the incidence of cardiovascular disease, diabetes, certain cancers, and depression. Medicinal approaches for obesity treatment have recently focused on looking at the hormonal regulation of appetite. The level of appetite in our bodies is controlled by peptide hormones which are released in the gut, such as oxyntomodulin (OXM).
OXM reduces appetite and food intake and increases the amount of energy the body uses. OXM is also known to increase the release of insulin (a hormone that helps control the levels of sugar in the body). The Study Drug, G3215, is chemically similar to OXM and is being investigated as a potential treatment for obesity and diabetes.

Who can participate?
Males aged 18 to 65 with a body mass index (BMI) between 25 and 38 kg/m² with either normal blood glucose levels, pre-diabetes or diabetes will be invited to participate in the study.

What does the study involve?
All participants will receive either the Study Drug or a placebo (saline), administered through an infusion pump (in the abdomen) continuously over a period of 14 days. The doses will vary depending on the group of participants, but will be administered incrementally (starting off at a low dose). As well as examining how safe and tolerable the Study Drug is, we will assess the participants blood glucose, body weight, energy intake and food intake. Participants will be invited back for follow up assessments to see when the Study Drug has cleared from their blood stream.

What are the possible benefits and risks of participating?
There will be no direct benefit from participating in the study. There will be no continued provision of any Study Drug or health intervention after the end of the study as the Study Drug is still being investigated for its safety. Although there may be no direct benefits of taking part, the results may lead to development of a treatment for obesity. Expected side effects of the Study Drug include temporary nausea and vomiting, and possibly skin reactions from wearing the pump or from taking blood samples.

Where is the study run from?
The study will be run from the NIHR/Wellcome Trust Imperial Clinical Research Facility (CRF) at the Hammersmith Hospital (UK). The study team is located at the Division of Metabolism, Digestion and Reproduction, Imperial College London at Hammersmith Hospital (UK).

When is the study starting and how long is it expected to run for?
January 2020 to October 2021

Who is funding the study?
The trial is being funded by a Divisional Research Funding Award from the Division of Women's, Children's and Clinical Support at Imperial College Healthcare NHS Trust, London (UK).

Who is the main contact?
Professor Tricia Tan, t.tan@imperial.ac.uk.

Contact information

Type(s)
Scientific

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Prof Tricia Tan

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-000051-12

Integrated Research Application System (IRAS)
278196

Study information

Scientific Title
A randomised, placebo controlled study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of an Oxyntomodulin analogue (G3215) delivered via a subcutaneous infusion in adult subjects

Study objectives
To investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of G3215 in adult subjects

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/06/2020, London - West London & GTAC Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 1048 007; westlondon.rec@hra.nhs.uk), ref: 20/LO/0411

Primary study design
Interventional

Study design
Double blind randomised placebo controlled ascending dose study in sequential groups at a single site

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetes Mellitus
Obesity

Interventions
Subjects will be randomised to 14 days of G3215 or placebo administered by continuous SC infusion over 14 days. The G3215 doses will be increased every 12/24 hours over the first four days, starting with 0.6 mg/24 hr in the first cohort.

Allocation to treatment will be according to a predetermined random order. The randomisation list will be generated using the Oracle Inform data capture system. This is a double-blind study. Randomisation of G3215 or placebo will take place for each group separately. The pair of sentinel subjects in Cohort 1 will be randomised such that 1 subject receives G3215 and 1 receives placebo.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
G3215 0.9% Saline [w/v] (placebo)

Primary outcome(s)
Safety and tolerability as assessed by:
1. Adverse events reported from the signing of the Informed Consent form until at least 5 half-lives or 7 days (whichever is longer) after the last dose of the study treatment

2. Vital signs: Blood pressure and pulse rate will be measured using an automated instrument with the subject in the supine position after resting comfortably for 10 minutes. Body temperature will be measured orally in degrees Celsius using an automated thermometer at screening and all inpatient and outpatient days. Additional monitoring can be added if deemed necessary for safety reasons
3. Physical examination performed by a physician and will include the examination of the following: general inspection chest/respiratory, heart/cardiovascular, gastrointestinal/liver, musculoskeletal/extremities, dermatological/ skin, thyroid/neck, lymph nodes, neurological /psychiatric at screening and all inpatient and outpatient visits. Additional monitoring can be added if deemed necessary for safety reasons
4. Clinical laboratory safety assessment is measured by the evaluation of blood and urine tests at screening and on every inpatient and outpatient study day. Additional and repeat testing may be performed at the discretion of the Principal Investigator
5. ECG parameters measured using computerised 12-lead ECG recordings after 5 minutes supine rest. Each lead shall be recorded for at least 3 beats at a speed of 25 mm/sec. The following parameters will be recorded: ventricular rate, PR interval, QRS duration, QT and QTc

Key secondary outcome(s)
Pharmacokinetics of the continuous subcutaneous infusion of G3215:
PK parameters will be calculated using the data from the GLP qualified LC-MS/MS assay. Pharmacokinetic (PK) parameters of the G3215 when infused continuously subcutaneously will include observed maximum concentrations (Cmax), time of occurrence of Cmax (tmax), area under the plasma concentration-time curve over 24 hr (AUC0-24h). Attainment of steady state will be investigated by visual assessment of plasma concentrations on those days where the final dose is administered.

Completion date
22/10/2021

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/09/2021:
1. Adult males aged 18 to 65 years inclusive with BMI between 25.0 and 45.0 kg/m² inclusive
2. Subjects may have normal glucose tolerance, Type 2 diabetes, impaired glucose tolerance or impaired fasting glucose according to WHO 2006 and 2011 criteria
3. The following criteria apply to subjects with Type 2 diabetes, impaired glucose tolerance or impaired fasting glucose according to WHO 2006 and 2011 criteria
3.1. They should be stably treated either with:
3.1.1. Diet and lifestyle changes only
3.1.2. Monotherapy with a sulphonylurea, metformin, or SGLT-2 inhibitor; or
3.1.3. Dual therapy with sulphonylurea/metformin, or sulphonylurea/SGLT-2 inhibitor
3.2. Patients treated with triple anti-diabetic treatments are excluded
3.3. The HbA1c at screening should be 6.0–8.5% (42–69 mmol/mol) and <±1.0% (±11 mmol/mol) from a previous HbA1c reading within the last 6 months, where available. Where an HbA1c reading within the last 6 months is not available, the subject should have HbA1c re-measured after at least 4 weeks to assure stability of glycaemia before inclusion in the study. This remeasurement may take place any time up to and including check in on Day -1
3.4. To allow assessment of eligibility, subjects without known diabetes or prediabetes, or in whom the glycaemic status is in doubt, may undergo a pre-screening visit no more than 10 weeks before Day 1 for assessment of fasting glucose, HbA1c and glucose 2 hours after a 75 g

oral glucose tolerance test
4. Subjects who are otherwise healthy enough to participate, as determined by pre-study medical history, physical examination and 12-lead ECG
5. Subjects whose clinical laboratory test results are either within the normal range or if outside this range the abnormalities are judged to be not clinically relevant and are acceptable to the Investigator
6. Subjects who are negative for hepatitis B surface antigen (HBsAg), hepatitis C antibody test and human immunodeficiency virus (HIV) I and II antibody tests at screening
7. Subjects who are negative for drugs of abuse and nicotine tests at screening and admissions
8. Subjects who do not take nicotine (including consumption of tobacco by any means or use of nicotine delivery systems) for at least 3 months preceding screening
9. Subjects who agree to use acceptable methods of contraception (see 7.2.3.1 and 7.2.3.2) for at least 3 months after study drug administration
10. Subjects who agree not to donate sperm for at least 3 months after study drug administration
11. Subjects who are able and willing to give written informed consent

Previous inclusion criteria:
1. Adult males aged 18 to 65 years inclusive with BMI between 25.0 and 38.0 kg/m² inclusive
2. Subjects may have normal glucose tolerance, Type 2 diabetes, impaired glucose tolerance or impaired fasting glucose according to WHO 2006 and 2011 criteria
3. The following criteria apply to subjects with Type 2 diabetes, impaired glucose tolerance or impaired fasting glucose according to WHO 2006 and 2011 criteria
4. They should be stably treated either with:
4.1. Diet and lifestyle changes only
4.2. Monotherapy with a sulphonylurea, metformin, or SGLT-2 inhibitor or
4.3. Dual therapy with sulphonylurea/metformin, or sulphonylurea/SGLT-2 inhibitor
4.4. Patients treated with triple anti-diabetic treatments are excluded
5. The HbA1c at screening should be 6.0–8.5% (42–69 mmol/mol) and <±1.0% (±11 mmol/mol) from a previous HbA1c reading within the last 6 months, where available. Where an HbA1c reading within the last 6 months is not available, the subject should have HbA1c re-measured after at least 4 weeks to assure stability of glycaemia before inclusion in the study. This remeasurement may take place any time up to and including check in on Day -1
6. To allow assessment of eligibility, subjects without known diabetes or prediabetes, or in whom the glycaemic status is in doubt, may undergo a pre-screening visit no more than 10 weeks before Day 1 for assessment of fasting glucose, HbA1c and glucose 2 hours after a 75 g oral glucose tolerance test
7. Subjects who are otherwise healthy enough to participate, as determined by pre-study medical history, physical examination and 12 lead ECG
8. Subjects whose clinical laboratory test results are either within the normal range or if outside this range the abnormalities are judged to be not clinically relevant and are acceptable to the Investigator
9. Subjects who are negative for hepatitis B surface antigen (HBsAg), hepatitis C antibody test and human immunodeficiency virus (HIV) I and II antibody tests at screening
10. Subjects who are negative for drugs of abuse, nicotine and alcohol tests at screening and admissions
11. Subjects who do not take nicotine (including consumption of tobacco by any means or use of nicotine delivery systems) for at least 3 months preceding screening
12. Subjects who agree to use acceptable methods of contraception for at least 3 months after study drug administration

13. Subjects who agree not to donate sperm for at least 3 months after study drug administration
14. Subjects who are able and willing to give written informed consent

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Male

Key exclusion criteria
1. Subjects who do not conform to the above inclusion criteria
2. Subjects who have a relevant history or presence of gastrointestinal (especially associated with vomiting), respiratory, renal, hepatic, haematological, lymphatic, neurological (especially if associated with balance disorders or vomiting e.g. migraine or labyrinthitis), cardiovascular, psychiatric, musculoskeletal, genitourinary, immunological, dermatological, connective tissue diseases or disorders that in the Investigator's opinion will compromise safety, practicability or scientific value of the study
3. Subjects who have a relevant surgical history that in the Investigator's opinion will compromise safety, practicability or scientific value of the study
4. Subjects who have used prescription drugs within 4 weeks of first dosing, with the following exceptions:
a. Anti-diabetic drugs as specified in the inclusion criteria.
b. Hypolipidaemic and/or antihypertensive treatments, provided that the doses have not been altered within the 4 weeks prior to entering the study.
c. Other medications may be allowed if the Investigator judges that they will not affect the outcome of the study or the safety of the subject.
5. Subjects who have used over the counter medication excluding routine vitamins and paracetamol but including megadose (intake of 20 to 600 times the recommended daily dose) vitamin therapy within 7 days of first dosing, unless agreed as not clinically relevant by the Investigator and Sponsor
6. Subjects who have a history of relevant and severe atopy e.g. asthma, angioedema requiring emergency treatment, severe hayfever requiring regular treatment (i.e. taking antihistamines and/or glucorticoids more regularly than 3 times a week), severe eczema requiring regular treatment (i.e. taking antihistamines and/or glucocorticoids more regularly than 3 times a week)
7. Subjects who have a history of relevant drug hypersensitivity
8. Subjects who have a history of alcohol abuse or alcohol dependence according to DSM-IV criteria within the last two years
9. Subjects who have a history of drug or substance abuse according to DSM-IV criteria within the last 2 years
10. Subjects who have a history of clinically significant migraine as judged by the Investigator. Subjects can be included if they have not had a migraine for the last 3 years

11. Subjects with a history of pancreatitis or pancreatic cancer
12. Subjects who consume more than 21 units of alcohol a week (unit = 1 glass of wine (125 mL) = 1 measure of spirits = ½ pint of beer)
13. Subjects who have a significant infection or known inflammatory process on screening
14. Subjects who have acute gastrointestinal symptoms at the time of screening or admission (e. g. nausea, vomiting, diarrhoea, heartburn)
15. Subjects who have an acute infection such as influenza at the time of screening or admission
16. Subjects who have donated blood within 3 months prior to screening
17. Subjects who have donated plasma within the 7 days prior to screening
18. Subjects who have donated platelets within the 6 weeks prior to screening
19. Subjects who have used any investigational drug in any clinical trial within 3 months of their first admission date
20. Subjects who have received the last dose of investigational drug greater than 3 months ago but who are on extended follow-up
21. Subjects who have previously received G3215
22. Subjects who have any dietary restrictions that, in the opinion of the Investigator, will compromise the safety, practicability or scientific value of the study
23. Subjects who cannot communicate reliably with the Investigator
24. Subjects who are unlikely to co-operate with the requirements of the study
25. History or evidence of abnormal eating behaviour, as observed through the Dutch Eating Behaviour (DEBQ) and SCOFF questionnaires at screening

Date of first enrolment
02/11/2020

Date of final enrolment
22/09/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Hammersmith Hospital
NIHR Imperial Clinical Research Facility
Imperial Centre for Translational and Experimental Medicine
London
United Kingdom
W12 0HS

Sponsor information

Organisation

Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Imperial College Healthcare NHS Trust: Division of Women's, Children's and Clinical Support

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/01/2024	18/01/2024	Yes	No
HRA research summary			28/06/2023	No	No