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Testing the safety and effects of a new study drug (GCG-06) in adult subjects (GCG-06 - first doses in human)

Submission date
22/07/2023

Recruitment status
No longer recruiting

Registration date
11/12/2023

Overall study status
Stopped

Last Edited
09/06/2026

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
This is a study of GCG-06 (the study medicine), an experimental new medicine for treating obesity. Obesity is a common problem and can lead to some serious and potentially life-threatening conditions, such as heart disease, type 2 diabetes and stroke. GCG-06 is similar to a naturally occurring hormone in the body called glucagon, which increases the level of sugar in the blood, reduces appetite, and increases how we burn fuel. It is hoped that the GCG-06 can be used together with other hormone-related medicines to help people eat less and reduce their body weight.

Who can participate?
Normal weight and overweight subjects, aged 18–70 years old

What does the study involve?
This is a 2-part study (Parts A and B). The study will test single and repeated doses of GCG-06, given by injection under the skin. It aims to find out its side effects and blood levels, its effect on body weight, and how the body handles glucose (a type of sugar) and amino acid (building blocks that make up protein).

In Part A, single doses of GCG-06 or placebo will be tested in up to 8 groups (42 participants in total). GCG-06 has never been given to humans before, so the starting dose will be small, and it will be increased as the study progresses. Participants will have 1 study session and take up to 3 weeks to finish the study. They will stay on the ward for 4 nights in a row and attend up to 3 outpatient visits.

In Part B, repeated doses of GCG-06 or placebo will be tested as 3 or 5 doses over 5 weeks, in up to 4 groups (32 participants in total). Participants will take about 10 weeks to finish the study. They will stay on the ward for up to 4 nights in a row on 1 occasion and up to 2 nights in a row on up to 4 occasions, and attend up to 6 outpatient visits.

What are the possible benefits and risks of participating?
To date, no humans have taken GCG-06, so its side effects are unknown. The study medicine has been thoroughly tested in laboratory animals. The highest dose that can be tested in this study is one that is predicted will give blood levels of the study medicine that were safe in animals.

Other medicines similar to the study medicine have been given to many people. The most common side effects are feeling sick (nausea), being sick (vomiting) and abdominal pain. As nausea and vomiting are expected to be the most common side effects, anti-emetics (anti-sickness medicine) will be available at the clinical unit.

Another side effect is high blood sugar (hyperglycaemia), so the participant's blood sugar level will be measured often. Hyperglycaemia tends to settle with time, but on rare occasions, this may result in the body breaking down fat cells excessively instead of sugar to produce energy, which can lead to an increased level of a chemical called ketone in the body. If a participant has hyperglycaemia, the study team will closely monitor the level of ketones in their blood and provide the appropriate level of care. In this study, participants will be closely monitored, and the dose of GCG-06 will not be increased unless the previous dose causes no important side effects. If a participant withdraws, they are asked to consent to a final follow-up. Consent is documented using an information and consent form (ICF), which has been approved by the HRA' s Generic Review Committee (GRC; REC ref: 18/GR/0054).

Like other similar medicines, reactions can occur at or near the site of injection. Symptoms might include redness, tenderness, itching and discomfort. Rarely, the study medicine might cause an allergic reaction, and result in more serious symptoms such as breathing difficulty, rash or low blood pressure up to 24 h after the dose. Participants will be closely monitored, to make sure they have not had a reaction. If they do have a reaction, appropriate medicine will be provided, as needed.

A volunteer's immune system might make antibodies against the study medicine. Those antibodies might stop the study medicine (or similar medicines) from working if they ever needed it in the future. In Part B, blood from participants in Group 1 will be tested to see if they make antibodies against the study medication.

During their stay, participants must follow HMR's 'house rules'. Our information leaflet is given to volunteers at screening and has been approved by the GRC (REC ref: 18/GR/0104).

If a participant's partner becomes pregnant during the study, they will be asked to contact their GP about the pregnancy – which is documented using a generic ICF that has been approved by the HRA's GRC (REC ref: 18/GR/0055 or 21/GR/16).

If any medically important problem is found at screening, the physician will tell the participant in person, and pass on the results to the participant's GP, using a letter template, which has been approved by the GRC (REC ref: 18/GR/0101).

The study team will contact participants' GPs to inform them that their patient has volunteered to participate in a study and provide the GP with a study summary. For first-in-human studies, the GP is asked if there is any medical problem that might compromise the volunteer's safety during the study. The GP letter templates have been approved by the GRC (REC refs: 18/GR /0098 and 18/GR/0099). Participants consent to the study team contacting their GP when they sign the ICF.

Please refer to the ICF(s) for Part A (version 2, dated 14 Nov 2023), and Part B (version 2, dated 14 Nov 2023), submitted with this application, for details on procedural risks, lifestyle and fasting restrictions, COVID-19 vaccine restrictions, and contraception requirements.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
July 2023 to May 2026

Who is funding the study?
Imperial College London (UK)

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

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2022-003579-40

Integrated Research Application System (IRAS)
1006692

Protocol serial number
2023/GCG-06/01

Study information

Scientific Title
A randomised, placebo-controlled first-in-human study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of GCG-06 in healthy normal weight/overweight subjects

Study objectives
To find out if GCG-06 has any important side effects when given as a single dose or as repeated doses to normal weight or overweight, but otherwise healthy, subjects.

To find out how much GCG-06 is absorbed into the bloodstream, and how long the body takes to get rid of it when given as a single dose and repeated doses.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/11/2023, South Central – Oxford A Research Ethics Committee (Temple Quay House, 2 The Square, Bristol Research Ethics Committee Centre, Bristol, BS1 6PN, United Kingdom; +44 (0)207 1048171; oxforda.rec@hra.nhs.uk), ref: 23/SC/0226

Primary study design
Interventional

Study design
Randomized placebo-controlled first-in-human study

Study type(s)
Efficacy, Safety

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

Interventions
Subjects will be randomised to GCG-06 or placebo, administered by subcutaneous (SC) injection.

Allocation to treatment will be according to a predetermined random order.

The trial will be in 2 parts:

Part A is a double-blinded, randomised, placebo-controlled, single ascending dose study (SAD), with the exception of cohort 1 which is partially blinded. These subjects will be overweight /obese but otherwise healthy volunteers. The planned starting dose is 0.1 mg.

Part B is a double-blind, randomised, placebo-controlled, multiple ascending dose (MAD) study in sequential groups of overweight/obese but otherwise healthy volunteers. Subjects in Part B will receive up to 5 doses of GLP-06/placebo by SC injection over a 29-day period, and have 5 inpatient stays, with a final follow-up visit 4-6 weeks post-last dose.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
GCG-06

Primary outcome(s)
The safety and tolerability will be assessed by the following measures:
1. Incidence and severity of adverse events (AEs) monitored continuously throughout the study
2. Changes in vital signs (blood pressure, pulse rate, temperature), 12-lead ECGs, physical examination, bedside glucose monitoring and local tolerability assessment to be monitored over the study period
3. Changes in clinical laboratory safety results monitored over the study period

Key secondary outcome(s)
Pharmacokinetic parameters (plasma) of GCG-06.

*Part A: Blood samples for assay of GCG-06 will be taken before dosing and frequently up to 12 h after dosing, on Days 2, 3, 4, and at each outpatient visit on Days 7 & 14 and at the final follow-up visit.

*Part B: In each TP, blood samples will be collected often during dosing days, on Day 30, on OP visits, and at the follow-up visit.

Completion date
12/05/2026

Reason abandoned (if study stopped)
Business reasons. The termination is not related to safety concerns.

Eligibility

Key inclusion criteria
1. Male and females of non-childbearing potential non-smokers aged 18-70 years old
2. Body mass index 20-30 kg/m2
3. In good health, as judged by medical history, medical examination, vital signs, ECG and clinical laboratory tests
4. Able to communicate with study personnel
5. Reliable, willing, and likely to comply with the protocol
6. Willing to comply with the contraception and gamete donation requirements of the protocol and consent to our informing their GP of their participation in the study, and to our entering their details into the over-volunteering database (TOPS).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
2

Key exclusion criteria
1. Unhealthy (clinically significant abnormality in our screening tests, which include ECG, vital signs, physical examination, and laboratory safety tests of blood and urine)
2. Diabetes or prediabetes
3. Abuse or have abused alcohol or drugs in the last 2 years
4. Drink, on average, more than 14 units of alcohol weekly
5. Have been treated by a doctor for severe allergic disease (such as severe asthma, severe hay fever requiring regular treatment, or severe eczema)
6. Currently taking certain medicines to treat diabetes
7. Taken prescription medicine during the 14 days before dosing; taken other medicine (except paracetamol or routine vitamins), herbal remedies or dietary supplements during the 7 days before the first dose; have had a serious reaction to any medicine
8. Have suffered from migraines in the last 3 years
9. Have a clinically relevant surgical history
10. Have had a serious reaction to any medicine
11. History of pancreatitis or pancreatic cancer
12. A history or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2
13. Have acute gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea, heartburn) at screening or admission
14. Have a current infection (such as flu)
15. Have had any condition or operation that might affect the way the body absorbs medicines
15. Have had any clinically significant disease
16. Taken GCG-06 in the past
17. Have a history or evidence of abnormal eating behaviour
18. Unwilling to comply with the contraception requirements of the protocol — because of the potential risk to babies conceived during the study
19. Have donated plasma in the 7 days before screening, blood in the 3 months before screening, or platelets in the 6 weeks before screening; have taken part in another clinical trial within 3 months before the first admission or are in the follow-up period of a clinical trial (where the last dose was taken more than 3 months before); or don't agree to donate blood, or take part in another study, during the 3 months after this study — because participants shouldn't expose themselves to unnecessary medicines more often than a few times a year, nor should they donate too much blood;
20. Objection by GP on medical grounds — because they might increase the risk, or confound the assessment of GCG-06; mental illness might compromise consent

Date of first enrolment

02/01/2024

Date of final enrolment
31/01/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
HMR
Cumberland Avenue
London
England
NW10 7EW

Sponsor information

Organisation
Zihipp Ltd.

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
University/education

Funder Name
Imperial College London

Alternative Name(s)
Imperial College of Science, Technology and Medicine, Imperial College London, UK, Imperial College London, London, England, Imperial College London in United Kingdom, imperialcollege, ICL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available