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Physiological study of kisspeptin in post-menopausal health

Submission date	Recruitment status	[X] Prospectively registered
11/06/2025	Recruiting	[_] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
16/06/2025	Ongoing	[_] Results
Last Edited	Condition category	[_] Individual participant data
18/07/2025	Nutritional, Metabolic, Endocrine	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

In women, menopause usually occurs between the ages of 45 and 55 years. It is a natural process during which the body stops producing female hormones (oestrogen and progesterone) and periods stop. This leads to a range of symptoms like anxiety, mood swings, sleep disturbances, vaginal dryness, hot flushes and “brain fog”. Menopause also increases the risk of developing long-term conditions, including Metabolic dysfunction-associated steatotic liver disease (MASLD), bone weakening (osteoporosis) and memory problems.

In MASLD fat builds up in the liver, and this can lead to inflammation, scarring, liver failure and liver cancer. MASLD affects about 1 in 3 adults in the UK and is the most common cause of liver transplants in women globally. Post-menopausal women are more susceptible to MASLD than men and younger women. Post-menopausal women are also at an increased risk of developing osteoporosis (thinning of the bones) which can lead to bone fractures. Additionally, menopause is often associated symptoms like 'brain fog', low mood and poor sleep.

Kisspeptin is a hormone produced in the brain, liver and other parts of our bodies. It regulates fertility in animals and humans, and animal studies suggest it may also help to reduce fat and inflammation in the liver. When Kisspeptin has been given to humans for short periods of time, it has positive effects on mood, behaviour and bone. Therefore, the aim of this study is to investigate the effect of kisspeptin on liver, bone and memory in post-menopausal women, when it is given for a longer period of time.

Who can participate?

We are looking for women-

• who are post-menopausal (i.e. women who have not had a menstrual period for at least 12 months with high levels of a hormone called follicle stimulating hormone) with abnormal liver function tests due to MASLD, and

• who are not taking medication or stable on medication (with no significant changes) for 3 months, and

• who have not had significant changes in their weight (i.e. up to ±6kg change in weight) for 3 months if they have not had bariatric surgery or stable weight for 12 months if they have had bariatric surgery in the preceding 24 months.

What does the study involve?
If you're interested, you'll first fill out a short questionnaire. If you're suitable, you'll be invited to a screening visit at Charing Cross Hospital. This includes a physical exam, blood tests, heart check (ECG), and a chance to ask questions.

After the screening visit, within 1 week, we will inform you if you can join the study. If you join the study, you will be randomly assigned to give yourself (at home) either kisspeptin, or a similar looking injection of salty water that has no medical effects (called a placebo), once a day for 12 weeks.

Before starting the injections at home, we will organise a visit during which you will complete some questionnaires and carry out some tasks assessing brain function (this visit will take up to 5 hours), as well as visits where several scans are carried out. These scans include an MRI and a Fibroscan (a special ultrasound scan) to look at your liver, and a special X-ray (DEXA scan) which will check the thickness of your bones. These scans will take place in one of the hospitals at Imperial College Healthcare NHS Trust in London.

You will be asked to attend the Clinical Research Unit at Charing Cross Hospital every other week from the start of the injections (i.e. weeks 1, 2, 4, 6, 8, 10, 12 – exact dates will be provided to you following the screening visit) and once after stopping the injections (i.e. week 24). On weeks 1, 6, 12, 24 you will attend longer study visits (up to 5 hours long) and the rest of the study visits will be much shorter (up to 3 hours long).

What are the possible benefits and risks of participating?
Kisspeptin may have beneficial effects while you are receiving the injections, although this is not yet known. Blood tests and scans may provide additional information about your health. Any significant abnormalities found will be discussed with you and, with your permission, your GP. Finally, your participation will help researchers understand the role of kisspeptin in post-menopausal women, which may lead to new treatments in the future.
The risks include:
-Injection-related side effects: These may include slight pain, minor bruising, or minimal bleeding at the injection site.
-Radiation exposure from DEXA scans: The DEXA scans involve low levels of ionising radiation. This adds only a very small increase to your lifetime risk of developing cancer (similar to having a chest X-ray).
-Unforeseen side effects: While no side effects have been observed in previous kisspeptin studies, unforeseen reactions are possible. You will be closely monitored by an experienced doctor at each visit.

Where is the study run from?
Imperial College London, UK

When is the study starting and how long is it expected to run for?
May 2024 to July 2029

Who is funding the study?
NIHR Biomedical Research Centre at Imperial College London (UK)

Who is the main contact?
The team can be contacted at imperial.kisspeptin@nhs.net

Contact information

Type(s)
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
335497

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Sponsor protocol's number 174676, CPMS 59000

Study information

Scientific Title
Physiological study of kisspeptin in post-menopausal health

Study objectives
Kisspeptin will have beneficial effects on liver fat and overall health in post-menopausal women.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/05/2025, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (2 Redman Place, London, London, EC20 1JQ, United Kingdom; +44 2071048096; cambsandherts.rec@hra.nhs.uk), ref: 25/EE/0077

Study design
Randomized double-blind placebo-controlled study

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Other

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Post-menopausal women who are at a higher risk of conditions affecting the liver, bone and brain.

Interventions
The eligible participants will be first invited to the screening visit. If they agree to join the study, they will be randomly assigned to give themselves subcutaneous (under the skin) injections of either kisspeptin 12.8nmol/kg, or placebo (sodium chloride), once a day for 12 weeks.

Prior to starting the injections at home, there will be a visit to complete some questionnaires and tasks assessing brain function, including cognition and mood (this visit will take up to 5 hours), as well as visits where several scans are carried out. These scans include an MRI and a Fibroscan (special ultrasound scan) and DEXA scan.

Then the participants will be asked to attend the Clinical Research Unit at Charing Cross Hospital every other week from the start of the injections (i.e. weeks 1, 2, 4, 6, 8, 10, 12 – exact dates will be provided to them following the screening visit) and once after stopping the injections (i.e. week 24).
On weeks 1, 6, 12, 24, they will attend longer study visits (up to 5 hours long). The rest of the study visits will be much shorter (up to 3 hours long).

An independent Statistical Consultant will use random number generating software to randomly allocate participant numbers in a 1:1 ratio to either the kisspeptin group or the placebo group prior to recruitment of the first participant. After recruitment, participants will be allocated a unique participant number in sequential order. An
independent researcher who will not be interacting with the participants nor be involved in the analysis of the results will receive the randomisation list from the statistician and will prepare the fortnightly sealed packs of either kisspeptin or saline (placebo).

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Physiological study using multi-method approach: physiological, behavioural and hormonal analyses

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Kisspeptin, Placebo (sodium chloride)

Primary outcome measure
Serum alanine transaminase (ALT, a marker of liver function) concentrations from baseline to 12 weeks of kisspeptin administration, measured using blood samples collected at each visit (total 8 visits) and analysed using standard laboratory techniques.

Secondary outcome measures
Other markers of liver function, including liver fat content from baseline to week 12 (as well as blood and urine markers), measured using blood samples collected at each visit (total 8 visits) and analysed using established laboratory techniques. Liver fat content will be measure using special MRI imaging in the beginning and end of the study.

Exploratory outcome measures:
A limited number of pre-specified exploratory outcome measures will be evaluated in sub-studies:
1. The percentage change in total osteocalcin concentration between baseline and week 12, measured using blood samples collected at each visit (total 8 visits) and analysed using established laboratory techniques.
2. Changes in markers of bone health (such as bone turnover markers and bone mineral density) from baseline to week 12, measured using blood samples collected at each visit (total 8 visits) and analysed using established laboratory techniques. Bone density will be measured using DEXA scans at the beginning and end of the study.
3. Changes in psychometric measures assessing various behavioural domains in postmenopausal health (including cognition, mood, anxiety, sociability, sexual function and quality of life) from baseline to week 12, using standardised psychometric questionnaires including WHQ, STA1-Y1, STAI-Y2, PHQ9, PANAS, MENQOL, FSFI, D2 test of attention, and Adapted Revise Cheek and Buss.

Overall study start date
01/05/2024

Completion date
31/07/2029

Eligibility

Key inclusion criteria
1. Women aged ≥40 years who are post-menopausal (i.e. absence of menstruation in the preceding 12 months with FSH levels in the post-menopausal range) as per STRAW criteria with metabolic dysfunction-associated steatotic liver disease (MASLD); and
2. Not taking any medication or stable on current medication for 3 months (i.e. no significant changes in dose,
formulation or route of administration); and
3. Stable weight (i.e. up to ±6kg change in weight) for 3 months if they have not had bariatric surgery or stable weight for 12 months if they have had bariatric surgery in the preceding 24 months.

Participant type(s)
Patient, Other

Age group

Adult

Lower age limit
40 Years

Upper age limit
80 Years

Sex
Female

Target number of participants
36

Key exclusion criteria
1. Current and recent medications that could affect study outcomes (e.g. GLP-1, hormonal treatments, bisphosphonates); including agents used in other interventional research studies within 3 months.
2. Consumption of >17.5 units (140g) alcohol intake/week for the previous 3 consecutive months prior to screening.
3. Evidence of cirrhosis, hepatic decompensation, or other chronic liver disease apart from MASLD, or if serum alanine aminotransferase or aspartate aminotransferase are more than five times the upper limit of normal.
4. Active malignancy or ongoing treatment for malignancy.
5. Anaemia Hb<11 g/dl or other biochemical abnormality that in the opinion of the investigators could interfere with study outcomes
6. History of fracture in the last 12 months (excluding hands and feet).
7. Active significant health condition which in the opinion of the research team might interfere with the potential participants' ability to participate and/or complete the study and/or might influence the study outcomes.
8. Taken part in any research study within the preceding 30 days (or 3 months if an investigational drug was administered)

Date of first enrolment
01/07/2025

Date of final enrolment
31/05/2029

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College London
Charing Cross Campus

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Sponsor information

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Sponsor type
University/education

Website
https://www.imperial.ac.uk

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
NIHR Imperial Biomedical Research Centre

Alternative Name(s)
NIHR Imperial BRC, Imperial Biomedical Research Centre, BRC

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal and presentation at national /international scientific conferences.

Intention to publish date
31/07/2029

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
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2	08/05/2025	11/06/2025	No	Yes
Participant information sheet	version 2	17/07/2025	18/07/2025	No	Yes