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IIH-Advance: A randomised clinical trial to determine the effects of weight loss, induced by a weight loss drug (Tirzepatide), in adults with active idiopathic intracranial hypertension

Submission date 15/01/2026	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 19/01/2026	**Overall study status** Ongoing	
Last Edited 15/01/2026	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

Idiopathic Intracranial Hypertension (IIH) is a condition where pressure inside the skull becomes too high. It mainly affects women of childbearing age who have obesity. This pressure can cause swelling at the back of the eye (called papilloedema), severe headaches, and sometimes permanent vision loss. There is no approved medicine for IIH, and current treatments are difficult to manage. Losing weight can help reduce the pressure and improve symptoms, but dieting is hard to maintain and surgery is not suitable for everyone. New medicines that help with weight loss, such as Tirzepatide, may offer a safer and easier option. This study aims to find out if Tirzepatide can help people with IIH by reducing weight and improving eye health.

Who can participate?

Adults aged 18 or over who have a confirmed diagnosis of IIH and swelling at the back of the eye (papilloedema) can take part. Participants need to have a body mass index (BMI) of 30 or more, or 27 or more if they have IIH linked to weight gain or belong to certain ethnic groups. They must have tried and failed to lose weight through dieting before. People who are pregnant, breastfeeding, have had certain surgeries, or have specific medical conditions cannot take part.

What does the study involve?

Participants will be randomly assigned to one of two groups. One group will receive Tirzepatide once a week using an injection pen, along with standard care. The other group will receive standard care only. The treatment will last for six months. Participants will give consent, self-administer the medication at home, and have their eye health checked using a scan called Optical Coherence Tomography (OCT) at a local Specsavers optician.

What are the possible benefits and risks of participating?

The main potential benefit is that weight loss from Tirzepatide may reduce the pressure inside

the skull, improve eye health, and reduce headaches. However, there are risks, including possible side effects from the medication such as nausea or other health issues. There is also a chance that symptoms may return if weight is regained after stopping the medication.

Where is the study run from?
University of Birmingham (UK), with eye scans carried out at Specsavers opticians.

When is the study starting and how long is it expected to run for?
January 2026 to October 2028

Who is funding the study?
Sir Jules Thorn Charitable Trust (UK)

Who is the main contact?
Prof Alexandra Sinclair, a.b.sinclair@bham.ac.uk
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Contact information

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Additional identifiers

Study information

Scientific Title
A phase III multi-stage randomised controlled trial to determine the effects of weight loss, induced by Tirzepatide, in adults with active idiopathic intracranial hypertension

Acronym
IIH-Advance

Study objectives
To evaluate the effect of weight loss induced by Tirzepatide plus standard of care over 6 months in patients diagnosed with IIH compared to standard of care only through the evaluation of the proportion of patients with resolution of papilloedema, measured by Optical Coherence Topography scan (OCT).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 29/10/2025, London - Central REC (3rd Floor 3 Piccadilly Place, London Road, Manchester, M1 3BN, United Kingdom; +44 207 104 8115; londoncentral.rec@hra.nhs.uk), ref: 347499

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Health services research, Supportive care, Treatment

Study type(s)

Health condition(s) or problem(s) studied
Idiopathic intracranial hypertension

Interventions
Design Overview
IIH-Advance is a phase III, multi-stage, randomised controlled trial designed to evaluate whether weight loss induced by tirzepatide improves disease activity in adults with active idiopathic intracranial hypertension (IIH). The trial uses a pragmatic, real-world approach, reflecting NHS practice while maintaining rigorous scientific standards.

Trial Structure
The study employs a two-arm parallel-group design with three sequential stages over a maximum of 18 months per participant:

Stage R1 (Months 0-6):
Participants are randomised 1:1 to tirzepatide plus standard care or standard care alone. This stage addresses the primary hypothesis: whether tirzepatide-driven weight loss increases the proportion of patients achieving papilloedema resolution at six months.

Stage R2 (Months 6-12):
Response-adaptive re-randomisation evaluates maintenance vs withdrawal and delayed initiation:
Responders to tirzepatide: continue vs stop treatment.
Non-responders to standard care: start tirzepatide vs continue standard care. This stage explores whether continued treatment sustains remission and whether late initiation still confers benefit.

Stage SA3 (Months 12-18):
Open-label tirzepatide for participants who have not yet received it,enabling assessment of recurrence and delayed response.

Population and Eligibility
N=86 adults with confirmed IIH (papilloedema on OCT),BMI ≥30 kg/m² (or ≥27 kg/m² with additional criteria),and at least one failed dietary attempt. Exclusions include recent bariatric surgery, prior IIH surgery, current glucose-lowering medication, recent GLP-1RA use and contraindications to tirzepatide.

Intervention
Participants allocated to active treatment will self-administer weekly tirzepatide injections, escalating from 2.5 mg to 15 mg over six months, with adjustments for tolerability. Standard care follows UK IIH guidelines (weight advice ± ICP-lowering medications).

Data Collection and Monitoring
All trial procedures are remote:
OCT scans at Specsavers.
Monthly video follow-ups for weight checks, adherence and safety.
Electronic data capture for questionnaires and diaries.
Bio sample kits and actigraphy devices mailed to participants.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
1. Resolution of papilloedema measured using OCT scan at 6 months

Key secondary outcome(s))

Completion date
31/10/2028

Eligibility

Key inclusion criteria
1. Confirmed diagnosis of IIH as defined by the IIH consensus criteria
2. Age 18 years or older
3. No evidence of sight-threatening papilloedema requiring urgent surgical intervention
4. Presence of papilloedema in at least one eye measured by OCT RNFL
5. Body Mass Index (BMI) greater than or equal to:
• 30.0 kg/sqm or
• 27.0 kg/sqm with IIH associated with increased weight or
• 27.0 kg/sqm and of South Asian, Chinese, other Asian, Middle Eastern, Black African or African Caribbean ethnicity*
6. At least one self-reported unsuccessful dietary effort to lose body weight
7. Able to provide written informed consent

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria

1. Previous bariatric surgery within the last 3 months or intention to undergo bariatric surgery during the trial
2. Previous surgery for IIH including optic nerve sheath fenestration, CSF shunting procedures, sub-temporal decompression and venous stenting
3. Using glucose-lowering medication
4. Currently taking or has received a GLP-1R agonist for any indication in the last 4 weeks
5. Previous or current pancreatitis
6. Contraindication to Tirzepatide (for example, previous or current medullary cancer, history of multiple endocrine neoplasia, active gall stones)
7. Current eating disorder requiring hospital intervention or treatment
8. Is unable to self-administer (or administer with carer support) the trial medication
9. Females of child-bearing potential only:
• Pregnant (spot urine test will be performed before randomisation to rule out pregnancy)
• Not willing to take highly effective contraceptive measures during the study intervention period AND for 5 weeks following the last trial medication dose
• Not willing to stop breastfeeding once randomised into the trial

Date of first enrolment
19/01/2026

Date of final enrolment
31/01/2027

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
University of Birmingham
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type

Funder Name
Sir Jules Thorn Charitable Trust

Alternative Name(s)
The Sir Jules Thorn Charitable Trust

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Requests for data generated during this study will be considered by BCTU (via bctudatashare@contacts.bham.ac.uk). Data will typically be available within six months after the primary publication unless it is not possible to share the data (for example: the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data).
Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BCTU Data Sharing Committee in discussion with the Chief Investigator and, where appropriate (or in absence of the Chief Investigator) any of the following: the Trial Sponsor, the relevant Trial Management Group (TMG), and independent Trial Steering Committee (TSC).
A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers transfer of patient identifiable information. Any data transfer will use a secure and encrypted method.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.0	27/11/2025	15/01/2026	No	Yes
Protocol file	version 1.0	03/09/2025	15/01/2026	No	No