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A study testing two medications, zibotentan and dapagliflozin, in people with high blood pressure

Submission date
17/06/2025

Recruitment status
Recruiting

Registration date
12/11/2025

Overall study status
Ongoing

Last Edited
12/11/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
High blood pressure, also known as hypertension, is a common condition and can increase the risk of heart attacks and strokes. Despite the availability of various medications, many people still have trouble keeping their blood pressure under control. Research suggests that about one-third of these patients do not reach their target blood pressure levels, even when taking medication.

This phase II study aims to find out if two medications, Zibotentan and Dapagliflozin, can effectively lower blood pressure in people with hypertension. Zibotentan blocks a protein called endothelin, which could relax blood vessels and lower blood pressure, but it can also cause the body to retain too much fluid. Dapagliflozin, a drug used to treat diabetes and heart failure, helps the kidneys remove sugar and water, which may reduce fluid build-up caused by Zibotentan.

Who can participate?
People with high blood pressure who are already taking at least two blood pressure medications will take part in this study at Cambridge University Hospital NHS Foundation Trust.

What does the study involve?
This is a randomised, placebo-controlled, double-blind, crossover study, meaning participants will receive both the actual medication combination and a placebo at different times during the study. They will be randomly assigned to either start with the actual medication and then switch to the placebo, or start with the placebo and then switch to the actual medication. Participants will make 9 visits to the research site over about 18 weeks for blood pressure checks, blood tests, and monitoring for side effects.

What are the possible benefits and risks of participating?
Patients who are not at target blood pressure (despite being on at least 2 antihypertensives) may benefit by helping to test a new combination drug therapy, which could help their blood pressure. This could lead to an improved understanding of whether this is of use in the future.

There's a risk of teratogenicity associated with Zibotentan should the female partner of a male participant fall pregnant during the study period. Therefore, we will only be recruiting women of non-childbearing potential and men who are surgically sterile, abstinent or agreed to use effective contraceptive methods with their partner during the study period.

Participants may experience discomfort in their arms due to the pressure of the cuff during blood pressure measurements at the clinic. To minimize this, the research team will use appropriately sized cuffs and will promptly stop the procedure upon the participant's request. Blood sampling may cause mild pain or discomfort at the site of the needle insertion. All blood draws will be performed by experienced and skilled healthcare professionals, aiming to achieve success on the first attempt. If necessary, the number of blood draw attempts will be limited to a maximum of three per visit. Lastly, participants may experience side effects from the investigational medicinal product. Participants will be provided with the research team's contact information to report any adverse effects immediately, allowing for timely clinical evaluation and decision-making. There is a time commitment associated with being part of a trial.

Where is the study run from?
Cambridge University Hospital NHS Foundation Trust, UK.

When is the study starting and how long is it expected to run for?
June 2025 to April 2027.

Who is funding the study?
NIHR Cambridge Biomedical Research Centre, UK.
AstraZeneca, UK.

Who is the main contact?
Dr Joseph Cheriyan, j.cheriyan@nhs.net

Contact information

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Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1010110

Study information

Scientific Title
Zibotentan and dapagliflozin in hypertensive patients- a pilot randomised controlled crossover clinical trial

Acronym
TRANSPARENT

Study objectives
To assess the on-treatment blood pressure-lowering effect of Zibotentan 1.5mg in combination with 10mg Dapagliflozin as compared to placebo.

To assess the on-treatment blood pressure-lowering effect of Zibotentan 0.75mg in combination with 10mg Dapagliflozin as compared to placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 04/09/2025, East of Scotland Research Ethics Service REC 2 (Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; -; tay.eosres@nhs.scot), ref: 25/ES/0051

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Crossover

Purpose
Treatment

Study type(s)
Efficacy, Safety

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

Interventions
This is a crossover study in which participants will be randomised via Sealed Envelope. Each participant will receive both the active treatment and a placebo in a randomised sequence over 12 weeks in total. Participants will begin with a lower dose of 0.75mg once daily for 4 weeks, followed by 1.5mg once daily for 2 weeks before crossing over to the alternate arm. All participants will be followed up two weeks after their final dose of the investigational medicinal product.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Zibotentan [Zibotentan, Zibotentan] , Dapagliflozin [Dapagliflozin propanediol]

Primary outcome(s)
Unattended seated automated office systolic blood pressure will be measured using a validated device at the end of each treatment period (Visit 5 and Visit 8)

Key secondary outcome(s))
The following secondary outcome measures are assessed using an automated sphygmomanometer, unless stated:
1. Unattended seated automated office diastolic blood pressure at the end of each treatment period (Visit 5 and Visit 8)
2. Unattended seated automated office systolic blood pressure after 28 days of each treatment period (Visit 4 and Visit 7)
3. Unattended seated automated office diastolic blood pressure after 28 days of each treatment period (Visit 4 and Visit 7)
4. Attended seated office systolic blood pressure at the end of each treatment period (Visit 5 and Visit 8)
5. Attended seated office diastolic blood pressure at the end of each treatment period (Visit 5 and Visit 8)
6. Attended seated office systolic blood pressure after 28 days of each treatment period (Visit 4 and Visit 7)
7. Attended seated office diastolic blood pressure after 28 days of each treatment period (Visit 4 and Visit 7)
8. Safety as assessed via adverse event and serious adverse event reporting at one timepoint

Exploratory outcome measures are assessed using an automated sphygmomanometer, unless stated:
1. Serum creatinine and eGFR using the CKD-EPI formula will be measured from venous blood sample and analysed through standardized laboratory methods at screening (visit 1), baseline (visit 2), week 4 (visit 4), week 6 (visit 5), week 10 (visit 7), week 12 (visit 8), and week 14 (visit 9)
2. HbA1C will be measured from venous blood sample and analysed through standardised laboratory method at screening (visit 1), baseline (visit 2), week 6 (visit 5) and week 12 (visit 8)
3. Serum alanine transaminase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) will be measured from venous blood sample and analysed through standardised laboratory method at screening (visit 1), baseline (visit 2), week 4 (visit 4), week 6 (visit 5), week 10 (visit 7), week 12 (visit 8), and week 14 (visit 9)
4. Weight will be assessed using standardised scale at screening (visit 1), baseline (visit 2), week 4 (visit 4), week 6 (visit 5), week 10 (visit 7), week 12 (visit 8), and week 14 (visit 9)
5. Body composition will be assessed using the InBody BWA 2.0 bioelectrical impedance analyser version at baseline visit (visit 2) and week 14 (visit 9)
6. Plasma aldosterone and renin will be measured from venous blood samples and analysed through standardised laboratory methods at screening (visit 1), baseline (visit 2), week 4 (visit 4), week 6 (visit 5), week 10 (visit 7), week 12 (visit 8), and week 14 (visit 9)
7. 24-hour ambulatory daytime mean systolic blood pressure after 4 weeks of each treatment period (Visit 4 and Visit 7)
8. 24-hour ambulatory daytime mean diastolic blood pressure after 4 weeks of each treatment period (Visit 4 and Visit 7)
9. 24-hour ambulatory mean systolic blood pressure after 4 weeks of each treatment period (Visit 4 and Visit 7)
910. 24-hour ambulatory mean diastolic blood pressure after 4 weeks of each treatment period (Visit 4 and Visit 7)

Completion date
30/04/2027

Eligibility

Key inclusion criteria
1. Clinical diagnosis of essential hypertension
2. Age 18 years or older
3. Seated attended office BP ≥140 and/or ≥90 mmHg.
4. Standardised home BP readings or daytime ambulatory BP of ≥130 and/or ≥80mmHg
5. Currently prescribed and taking at least two antihypertensive drugs at screening
6. eGFR >45ml/min/1.73m2 at screening
7. Capable of providing signed informed consent
8. Female of non-child bearing potential
9. Male being surgically sterile, abstinent or willing to use in conjunction with their female partner, a highly effective method of contraception
10. Willingness to comply with double contraception method (applied to men)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Women of childbearing potential or those who are pregnant, breast-feeding, or women with intent of getting pregnant.
2. Confirmed secondary cause of hypertension (e.g. renal artery stenosis, adrenal adenoma, phaeochromocytoma etc)
3. Seated attended office systolic BP ≥180 or diastolic BP ≥ 110 mmHg
4. Active planning for pregnancy during the trial (applicable to both men and women)
5. Current or prior medical treatment with an ETA antagonist or SGLT2 inhibitor
6. Known acute coronary syndrome within 3 months of screening visit
7. Unstable heart failure requiring hospitalisation within last 6 months at screening visit
8. Known heart failure with New York Heart Association (NYHA) classification of III or IV
9. Uncontrolled diabetes (HBA1C within last 3 months from screening >12%)
10. Known Type 1 diabetes
11. Known Type 2 diabetes on insulin
12. Participants treated with strong CYP3A4 inhibitor
13. Screening blood pressure indicating hypotension (systolic BP < 90 mmHg or diastolic BP < 60 mmHg)
14. Male in a sexually active relationship with pregnant or breastfeeding partner
15. History of transplantation (other than corneal)
16. Severe hepatic impairment at screening (ALT > 3 ULN)
17. Positive drugs of abuse test at screening
18. History of alcohol abuse at screening
19. Known clinical diagnosis of hepatitis or HIV
20. Participants with a known hypersensitivity to Dapagliflozin or Zibotentan or any of the excipients of the product
21. Participation in another clinical study involving a study intervention or investigational medicinal device within the past 30 days, or for investigational drugs, within 5 half-lives (whichever is longer) prior to the first dose in this trial

Date of first enrolment
25/10/2025

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
-
-
NO COUNTRY SPECIFIED, assuming England
England
-

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
NIHR Cambridge Biomedical Research Centre

Alternative Name(s)
Cambridge Biomedical Research Centre, NIHR Cambridge BRC, National Institute for Health Research Cambridge Biomedical Research Centre

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Specific requests may be considered on an individual basis and reviewed by the Chief Investigator, subject to appropriate approvals from funders.

Formal data sharing agreements will be established with any collaborating researchers or institutions. These agreements will detail the terms of use, data handling practices, and confidentiality obligations. Access to the data will be controlled through a secure authorization process, ensuring that only authorized personnel can access the information.

Data will be stored and transmitted using encrypted methods to safeguard against unauthorized access. We will comply with all relevant regulations, including GDPR and other applicable data protection laws, and will obtain any necessary approvals from regulatory bodies or ethics committees.

The data sharing process will be monitored through regular audits and compliance checks to ensure adherence to ethical standards and agreements. Participants will retain the right to inquire about the use of their data and to withdraw consent if they choose to do so.

The trial database is held in MACRO, which is hosted by the trial sponsor. Personally identifiable data will be kept as part of the patient's health record at the sponsor site and will only be accessible by delegated team members. The trial dataset will be retained for up to 5 years after the end of the trial as per the regulatory framework. Any trial data that may be shared will be de-identified, and personally identifiable data will not be sent. Participants will consent to their de-identified data being shared and are able to withdraw consent for this at any time.

IPD sharing plan summary
Available on request, Stored in non-publicly available repository