ISRCTN40182296 https://doi.org/10.1186/ISRCTN40182296

A clinical trial to assess if drug-coated balloons are an effective treatment for arteriovenous fistulas in patients on haemodialysis

Submission date
01/08/2023

Recruitment status
Recruiting

Registration date
04/08/2023

Overall study status
Ongoing

Last Edited
01/11/2024

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Fistulas used for haemodialysis commonly develop narrowings that affect their function. These are treated with a balloon which is inflated to widen the narrowing. The narrowings often come back after this treatment. Balloons are now available that are coated with drugs called paclitaxel and sirolimus. Some evidence suggests these balloons may prevent the narrowing of fistulas from coming back. This study will tell us if this is true.

Who can participate?
Patients aged 18 years and over receiving treatment with haemodialysis who need a balloon treatment to their fistula

What does the study involve?
Participants will be randomly allocated to receive treatment (under X-ray guidance) with either a paclitaxel-coated balloon, sirolimus-coated balloon, or a similar uncoated balloon straight away. In some hospitals, patients will also be invited to have an ultrasound scan of their fistula before, immediately after, and 3 months after the balloon treatment. Following the second balloon treatment, a member of the study team will talk to the participants every 3 months for 1 year and collect information. No additional visits are essential for taking part in the study. Participants will also be asked to complete a questionnaire about how they are coping with day-to-day activities. The researchers will also ask for permission to use any information that is stored in medical case notes or on the hospital databases for the study duration (1 year). The study makes no provision for the use of drug-coated balloons after the study has ended.

What are the possible benefits and risks of participating?
The researchers cannot promise that this study will help, but this is an opportunity to take part in some important research that may help improve the future treatment of people on haemodialysis. There are no significant disadvantages. There should be no significant additional pain or discomfort due to taking part in the study. The drug on the balloon is not absorbed in large amounts. Some of the procedures may be extra to those that participants would have if they did not take part. These procedures use ionising radiation to form images of the body, to

provide treatment and provide the doctor with other clinical information. Ionising radiation may cause cancer many years or decades after exposure. We are all at risk of developing cancer during our lifetime: 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study may increase the chances of this happening to about 50.03% i.e., a very small increase.

Where is the study run from?
1. Guy's and St Thomas' NHS Foundation Trust (UK)
2. King's College London (UK)

When is the study starting and how long is it expected to run for?
December 2021 to December 2027

Who is funding the study?
1. National Institute for Health Research (UK)
2. Medical Research Council (UK)

Who is the main contact?
Dr Michael Robson, michael.robson@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Chloe Spriggs

Contact details
M2.06 (Clinical Trials Unit)
IoPPN
16 De Crespigny Park
London
United Kingdom
SE5 8AF
+44 (0)20 7848 0532
Chloe.spriggs@kcl.ac.uk

Type(s)
Scientific

Contact name
Dr Michael Robson

ORCID ID
http://orcid.org/0000-0002-1192-1353

Contact details
Guy's Hospital
London
United Kingdom

SE1 9RT
+44 (0)207 188 7188
michael.robson@kcl.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
323715

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 57281, IRAS 323715

Study information

Scientific Title
Paclitaxel or sirolimus coated balloons used for ArterioVEnous fistulas - 2 (PAVE-2 trial): a randomised controlled clinical trial to determine the efficacy of paclitaxel or sirolimus coated balloons in arteriovenous fistulas used for haemodialysis

Acronym
PAVE-2

Study objectives
The hypothesis is that paclitaxel-coated and/or sirolimus-coated balloons will prolong the time to loss of patency of a treatment segment (segment of vein treated with a fistuloplasty) in arteriovenous fistulas used for haemodialysis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/07/2023, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8345; hampstead.rec@hra.nhs.uk), ref: 23/LO/0625

Study design
Randomized; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Arteriovenous fistulas for haemodialysis

Interventions
Current intervention as of 07/08/2023:
Following the clinically-indicated fistuloplasty, patients will be allocated by chance into one of the three groups. Fistulas will be treated with paclitaxel-coated balloons, sirolimus-coated or balloons or uncoated balloons. Participants will be followed up for 1 year to assess the primary and secondary endpoints indicated below.

_____

Previous intervention:
DESIGN AND METHODOLOGY
Patients who agree to take part will be allocated by chance into one of the three groups. Fistulas will be treated with (1) paclitaxel-coated balloons (2) sirolimus-coated balloons or (3) uncoated balloons. The researchers will compare the outcomes for each of the two groups treated with paclitaxel or sirolimus-coated balloons with the control group who were treated with uncoated balloons. They will follow up for 1 year and see how long it takes for the fistula to block or for the patient to need another balloon treatment.

SUMMARY OF WHAT WILL HAPPEN TO PARTICIPANTS
1. After potential participants have read the information sheet, had the opportunity to ask questions, and given written consent we will check that they fit the criteria to take part in the study.
2. They will then have a balloon treatment to their fistula which is needed for medical reasons, whether they are taking part in this study or not.
3. Following the clinically-indicated balloon treatment, inclusion and exclusion criteria will be checked again, including a residual stenosis of less than 30% (indicating a successful procedure). If the participant remains eligible they will be randomised to one of three groups.
4. Participants will receive a second treatment (under X-ray guidance) with either a paclitaxel-coated balloon, sirolimus-coated balloon, or a similar uncoated balloon straight away.
5. In some hospitals, patients will also be invited to have an ultrasound scan of their fistula before, immediately after, and three months after the balloon treatment. If someone does not wish to have the ultrasound scans they can still take part in the rest of the research study.
6. Following the second balloon treatment, study visits will occur every 3 months for 1 year. No additional visits are essential for taking part in the study. We will avoid additional travel by talking to patients on the telephone. Data recorded for each study assessment will include target lesion primary patency, access circuit primary patency, time to AVF abandonment, access

circuit interventions, access circuit dysfunction, and adverse events.
7. Participants will also be asked to complete questionnaires about how they are coping with day-to-day activities at baseline, 6-, and 12-months post-randomisation.

END OF STUDY
End of study is defined as last participant last follow-up.

PILOT AND INTERIM ANALYSIS
An internal pilot will consider recruitment rates at 9 months and formal interim analyses will be conducted when 33% and 66% of expected total follow-up data are available. Based on the interim analyses the Trial Steering Committee may recommend stopping one or more trial arms early.

MEASURES TO AVOID BIAS
A fully blinded trial is not possible due to the differing appearances of the balloons. The only people who will be aware of the treatment allocation are the treating radiologist and the trial manager (for monthly balloon re-stocking purposes). The patient, clinical team and research team (including trial statisticians) will remain blinded to treatment allocation.

Referral for a repeat procedure will originate from the clinical team who are unaware of treatment allocation.
A different radiologist to the one performing the index procedure will perform repeat procedures when possible but it is not possible to guarantee this. Therefore, the radiologist performing the repeat procedure may have knowledge of whether the patient was treated with a particular drug-coated or uncoated balloon.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
IN.PACT (Medtronic, paclitaxel-coated balloon) and MagicTouch (Concept Medical, sirolimus-coated balloon)

Primary outcome measure
Time to end of treatment segment primary patency (TSPP). TSPP ends when any of the following occurs: (a) clinically driven re-intervention to the treatment segment; (b) thrombotic occlusion considered to be due to restenosis at the treatment segment; (c) surgical intervention that excludes the treatment segment from the access circuit; (d) abandonment of the AVF due to an inability to retreat the treatment segment.

Secondary outcome measures
1. Time to loss of primary patency at any treatment segment
2. Time to end of access circuit primary patency. Access circuit primary patency ends when any of the following occurs: (a) access circuit thrombosis, (b) an intervention (either radiological or surgical) anywhere in the access circuit, or (c) the AVF is abandoned due to an inability to treat

any lesion.
3. Time to AVF abandonment. AVF abandonment occurs when the AVF is abandoned, regardless of radiological or surgical intervention, with or without a thrombosis event. Multiple/repetitive treatments for stenoses that restore patency are compatible with cumulative patency.
4. Number of radiological or surgical interventions
5. Adverse events (e.g. thrombosis, infection localised to AVF, rupture of AVF)
6. Intima-media thickness and degree of stenosis measured using ultrasound at 3 months
7. Patient quality of life assessed by EQ-5D-5L and VASQoL at 6 and 12 months

Overall study start date
06/12/2021

Completion date
31/12/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/05/2024:
1. Patients (18 years or over) who have a surgically formed AVF in the arm which has been used for at least 8 dialysis sessions in the preceding 4 weeks
2. An indication for a fistuloplasty as determined by the local clinical team
3. The access circuit is free of synthetic graft material or stents
4. Patient able to give informed consent
5. Patient willing and able to comply with all study-related procedures
6. People who are not breastfeeding, not pregnant, not intending to become pregnant or not intending to father children, within two years of study treatment
7. No evidence of active systemic or local (to the fistula) infection
8. No known hypersensitivity or contraindication to contrast medium which cannot be adequately premedicated
9. No known hypersensitivity or contraindication to paclitaxel or sirolimus
10. One or two treatment segments. Each treatment segment will contain one or more stenoses of at least 50%
11. Each treatment segment will be amenable to treatment with a single drug-coated balloon 8cm in length or two overlapping drug-coated balloons 4 cm in length

Previous inclusion criteria:
1. Patients (18 years or over) who have an AVF in the arm which has been used for at least 8 dialysis sessions in the preceding 4 weeks
2. An indication for a fistuloplasty as determined by the local clinical team
3. The access circuit is free of synthetic graft material or stents
4. Patient able to give informed consent
5. Patient willing and able to comply with all study-related procedures
6. People who are not breastfeeding, not pregnant, not intending to become pregnant or not intending to father children, within two years of study treatment
7. No evidence of active systemic or local (to the fistula) infection
8. No known hypersensitivity or contraindication to contrast medium which cannot be adequately premedicated
9. No known hypersensitivity or contraindication to paclitaxel or sirolimus
10. One or two treatment segments. Each treatment segment will contain one or more stenoses of at least 50%

11. Each treatment segment will be amenable to treatment with a single drug-coated balloon 8cm in length or two overlapping drug-coated balloons 4 cm in length

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 642; UK Sample Size: 642

Key exclusion criteria
1. Thrombosed (failed) access circuit at time of treatment
2. Location of a stenosis central to the thoracic inlet
3. The presence of a lesion that has been treated with a plain balloon fistuloplasty where the diameter of the outflow vein is larger than the size of the largest available drug-coated balloon
4. The presence of a lesion that has been treated with a plain balloon fistuloplasty where the diameter of the outflow vein is considered too small to be treated with the smallest available drug-coated balloon
5. A significant residual stenosis (more than 30%) at any treated lesion after plain balloon fistuloplasty
6. Lack of availability of any of the three types of treatment balloon (Medtronic IN.PACT, Concept Medical MagicTouch or control) at the required size

Date of first enrolment
06/05/2024

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre

Guys Hospital
Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Lister Hospital
Coreys Mill Lane
Stevenage
United Kingdom
SG1 4AB

Study participating centre
Queen Elizabeth Hospital
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Kent and Canterbury Hospital
Ethelbert Road
Canterbury
United Kingdom
CT1 3NG

Study participating centre
St Helier Hospital
Wrythe Lane
Carshalton
United Kingdom
SM5 1AA

Study participating centre
Gloucestershire Royal Hospital
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Queen Alexandras Hospital
Southwick Hill Road
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre

Manchester Royal Infirmary
Cobbett House
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Hammersmith Hospital
Du Cane Road
Hammersmith
London
United Kingdom
W12 0HS

Study participating centre
Royal London Hospital
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
United Kingdom
G51 4TF

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Preston
United Kingdom
PR2 9HT

Sponsor information

Organisation

King's College London

Sponsor details
Strand
London
England
United Kingdom
WC2R 2LS
+44 (0)207 8487306
vpri@kcl.ac.uk

Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

ROR
https://ror.org/0220mzb33

Organisation
Guy's and St Thomas' NHS Foundation Trust

Sponsor details
Guy’s Hospital,
Great Maze Pond,
St Thomas’ Hospital,
Westminster Bridge Road
London
England
United Kingdom
SE1 7EH
-
R&D@gstt.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.guysandstthomas.nhs.uk/Home.aspx

ROR
https://ror.org/00j161312

Funder(s)

Funder type

Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR151282

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2028

Individual participant data (IPD) sharing plan
The datasets analysed during the current study will be made available following any reasonable application to Michael Robson (Michael.robson@kcl.ac.uk) following the primary publication for the trial.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		31/10/2024	01/11/2024	Yes	No