ISRCTN30648419 https://doi.org/10.1186/ISRCTN30648419

Clopidogrel, aspirin and rivaroxaban after a medical procedure used to widen narrowed or blocked arteries using a balloon or stent

Submission date
28/06/2024

Recruitment status
Recruiting

Registration date
22/08/2024

Overall study status
Ongoing

Last Edited
22/01/2025

Condition category
Circulatory System

[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
Blocked leg arteries, often caused by diabetes or smoking, are increasingly common and can result in potentially severe consequences like amputation or even death if left untreated. In the UK, between 16,500 and 30,000 people die and 3,500 face amputations due to heavily blocked leg arteries annually. Each year, over 4,000 angioplasty medical procedures are conducted in the UK to widen narrowed or blocked arteries using a balloon or stent. After an angioplasty, patients typically receive medications known as “blood thinners” to prevent blood clots and lower the chance of needing an amputation. Despite the widespread use of various tablet combinations by vascular surgeons in the UK, the optimal blood thinners for effectiveness and safety remain unknown.
This research will compare three commonly used blood thinners after angioplasty: Clopidogrel alone, Aspirin and Clopidogrel, and Aspirin and Rivaroxaban. The research will be ‘randomised’, meaning that patients will be randomly chosen by a computer to receive one of the three treatments, ensuring equal chances for each. Everything else will be the same.
The research aims to determine the optimal blood thinners for preventing complications of blocked arteries after angioplasty without causing too much bleeding. The research will also assess how much value these treatments provide in terms of their cost for the National Health Service (NHS). The results are expected to help improve the care of many patients needing angioplasty in the future.

Who can participate?
This research will involve roughly 20 vascular units in the UK, with 1,239 participants undergoing angioplasty in the lower leg due to blocked arteries.

What does the study involve?
Within 10 days of angioplasty, participants will start taking the assigned blood thinners for up to three years. We will ask participants about their quality of life and will be monitored for health problems such as further blockages, amputations, heart attacks, strokes and serious bleeding.

What are the possible benefits and risks of participating?
Benefits:
By participating in this trial, you will be helping us to answer questions about the optimal blood-thinners after angioplasty in the lower leg that may result in better care for patients needing this in the future. We know patients who are enrolled in randomised trials tend to do better medically than those who are not, probably because they have more points of contact with the hospital.
Risks:
The major burden on participants is the time taken to complete pain and quality of life questionnaires at baseline and 2, 6 and 12 months and possibly at 24 and 36 months after their procedure. While there are potential risks to taking the medicinal products, the risk is no higher than the risk of standard medical care. These medicines will be used within the licensed range of indications, dosage and form, and are all and are all currently used in UK clinical practice to all patients after endovascular intervention to reduce the risk of subsequent ischaemic events such as acute limb ischemia or myocardial infarction outside of the trial. The known and most commonly anticipated safety issue is bleeding risk. To minimise risks, patients at risk of increased bleeding will be excluded. E.g. patients with pre-existing indication for dual antiplatelet therapy or anticoagulant (atrial fibrillation and inherited and acquired bleeding disorders), open bypass as part of hybrid procedure, , active malignancy or any other non-vascular condition associated with a life expectancy of less than 36 months, embolic arterial disease, non-atherosclerotic Peripheral Arterial Disease (PAD), renal failure with creatinine clearance <15ml/minute.

Some patients have arterial disease in more than one territory (e.g. peripheral arterial disease and coronary artery disease; polyvascular disease) and are known to be at higher risk of both ischaemic and bleeding events. The bleeding risk of some patients with polyvascular disease will exclude them from CLARITY PAD.

Patients taking anticoagulants are to be carefully observed for signs of bleeding. Major bleeding is our primary safety outcome and other bleeding outcomes will be followed up as secondary outcome measures. The anticipated safety issues will be addressed within normal clinical practice.
Patients will be monitored for signs of bleeding and treatment should be stopped if severe bleeding occurs. In addition to restrictive eligibility criteria, other risk mitigation strategies include trial oversight from the Trial Management Group (TMG), Independent Data Monitoring Committee (IDMC) and Trial Steering Committee (TSC).

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
June 2024 to December 2028

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Clarity-Trial@cardiff.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Wakunyambo Maboshe

Contact details
Centre for Trials Research, 7th Floor, Neuadd Meirionnydd, Heath Park
Cardiff
United Kingdom
CF14 4YS
+44 29 20687457
maboshew1@cardiff.ac.uk

Type(s)
Scientific, Principal investigator

Contact name
Mr Christopher Twine

Contact details
Southmead Hospital, Southmead Road, Westbury-on-Trym
Bristol
United Kingdom
BS10 5NB
+44 1174 4140826
christopher.twine@bristol.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007268

Protocol serial number
R&D 5410, IRAS 1007268

Study information

Scientific Title
CLopidogrel, Aspirin and RIvaroxaban after revascularisation with angioplasTY for limb-threatening Peripheral Arterial Disease (CLARITY PAD)

Acronym
CLARITY PAD

Study objectives

Primary objective:
To compare the clinical effectiveness of three commonly used antithrombotic regimens (clopidogrel; aspirin plus clopidogrel; aspirin plus low-dose rivaroxaban) following endovascular intervention for CLTI

Secondary objectives:
1. To evaluate the effect of three commonly used antithrombotic regimens on major adverse limb events, major adverse cardiovascular events, major bleeding, minor bleeding, primary and secondary patency of artery, reintervention, healing of tissue loss, health-related quality of life, resource use and costs.
2. To evaluate the delivery of the CLARITY trial and trial interventions through qualitative process evaluation

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 21/08/2024, Wales REC 5 (Castlebridge 4, 15-19 Cowbridge Rd E, Cardiff, CF11 9AB, United Kingdom; +44 2921 052459; Wales.REC5@Wales.nhs.uk), ref: 24/WA/0211

Study design
Pragmatic adaptive multicentre open-label three-arm individually randomized controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Antithrombotic treatment after percutaneous or hybrid endovascular intervention for chronic limb-threatening ischemia of the lower limbs

Interventions
Oral course (up to 36 months) of one of the following treatments:
1. A 75mg clopidogrel tablet taken once daily
2. Dual antiplatelet therapy with a 75mg aspirin tablet and 75mg clopidogrel tablet, both taken once daily
3. Dual antiplatelet therapy with a 75mg aspirin tablet taken once daily and a 2.5mg rivaroxaban tablet taken twice daily

Participants in all trial arms will be followed up within 2-months of the procedure, at 6 months and annually post-procedure.
Treatment and follow-up duration will range between 1 year and 3 years depending on when the participant joins the trial.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Aspirin, clopidogrel besilate, rivaroxaban

Primary outcome(s)
A composite event-free survival time of:
1. Acute limb ischaemia
2. Major lower limb amputation
3. Myocardial infarction
4. Ischaemic stroke
5. All-cause mortality
Measured using patient records at 2 months, 6 months, 12 months, 24 months and 36 months

Key secondary outcome(s))
Measured via case report forms (CRFs) or questionnaires either from patient notes or directly from participants at 2 months, 6 months, 12 months, 24 months and 36 months:
1. Major adverse limb events (MALE) (defined as amputation or major reintervention of the trial limb)
2. Major adverse cardiovascular events (MACE) (defined as recurrent CLTI, amputation affecting contralateral limb, acute coronary syndrome, ischaemic stroke)
3. Bleeding Academic Research Consortium (BARC 2, 3 or 5) and Thrombolysis In Myocardial Infarction (TIMI) defined major bleeding
4. Minor bleeding
5. Primary and secondary patency of artery
6. Reintervention
7. Healing of tissue loss
8. Health-related quality of life (VascuQoL and EQ-5D-5L)
9. Cost-effectiveness
10. Qualitative process evaluation

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Adults (aged 18 years and over) undergoing percutaneous or hybrid endovascular intervention for CLTI of the lower limbs
2. Atherosclerosis as the cause of CLTI
3. Target arteries: infrainguinal (common femoral to pedal) if percutaneous, or iliac to pedal if performed as part of hybrid revascularisation with common femoral endarterectomy
4. Clinicians would use trial antithrombotic combinations in normal clinical practice
5. Able to provide informed consent
6. First time in the CLARITY trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Open lower-limb bypass as part of hybrid procedure
2. Pre-existing clinical indication for dual antiplatelet therapy or anticoagulant e.g. atrial fibrillation
3. Active malignancy or any other non-vascular condition associated with a life expectancy of less than 36 months
4. Patients undergoing intervention to treat asymptomatic restenosis of a lower-limb bypass graft
5. Embolic arterial disease
6. Renal failure with creatinine clearance <15ml/minute
7. Thrombophilia or any other inherited or acquired bleeding disorders
8. Persons of childbearing potential who have a positive pregnancy test, are breastfeeding or attempting pregnancy

Date of first enrolment
14/01/2025

Date of final enrolment
30/06/2027

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre

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

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
St Georges University Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

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

Study participating centre
St Marys Hospital
St. Marys Hospital
Floyd Drive
Warrington
United Kingdom
WA2 8DB

Study participating centre
Northern General Hospital
Northern General Hospital NHS Trust
C Floor, Huntsmnan Building
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
North Bristol NHS Trust

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes