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Is there a rebound increase in platelet aggregation following withdrawal of aspirin or ticagrelor in patients who have recently undergone PCI?

Submission date
11/02/2015

Recruitment status
No longer recruiting

Registration date
18/02/2015

Overall study status
Completed

Last Edited
06/08/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Coronary angioplasty is a procedure which widens coronary arteries that have become narrowed or blocked, due to fatty deposits on the inner arterial wall. A small balloon is fed though to the affected section of an artery and inflated to widen the artery and squash the fatty deposits against the wall. The balloon is then deflated and removed and the result is an increased blood flow though the artery. Sometimes, a stent is used. This expands when the balloon is inflated and remains in place once the balloon is used. Most people will need to take blood thinning medications after an angioplasty. For many patients who have a stent inserted the combination of blood thinning medication that is given is clopidogrel and aspirin. Typically this is given in combination for 12 months and, thereafter, aspirin is given alone. Recently, a new blood thinning drug, ticagrelor, has been developed. A large clinical study has shown that a combination of ticagrelor and aspirin has been shown to work better than clopidogrel and aspirin. Currently, NHS patients only receive ticagrelor in combination with aspirin. However, in a laboratory setting, ticagrelor has been shown to be a very potent 'blood thinner'. This may mean that in some patients aspirin is not needed which may be beneficial as aspirin can cause problems such as bleeding. In the GLOBAL LEADERS study patients have been randomly allocated to stop aspirin at one month and continue with ticagrelor or stop ticagrelor at 12 months and continue with aspirin. This is a substudy of the GLOBAL LEADERS trial which aims to see if the ability of the blood to clot is different when aspirin is stopped, compared with when ticagrelor is stopped. We will also measure a chemical called thromboxane; a molecule that increases blood clotting. The production of thromboxane is reduced by both ticagrelor and aspirin. In order to make this measurement blood may be stored for a few weeks or months before this test is carried out following which it will be disposed of as per normal practice. No genetic testing will be undertaken. The aim of this trial is to evaluate whether there is a difference in the likelihood of the blood to clot when aspirin is withdrawn at 1 month versus when ticagrelor is withdrawn at 12 months. A better understanding of clotting after withdrawal of these drugs may allow us to further develop better treatment strategies for patients suffering from heart disease.

Who can participate?
Adults (aged at least 18) enrolled in the the GLOBAL LEADERS study under the care of the Golden Jubilee National Hospital (UK) during the allocated study period with a narrowing of one or more coronary arteries suitable for coronary angioplasty using a stent.

What does the study involve?
Two groups of participants take part in the study. One group (group 1) have been previously randomised to change from ticagrelor and aspirin to just ticagrelor 1 month following a coronary angioplasty involving a stent. Group 2 includes participants previously randomised to switch from ticagrelor and aspirin to just aspirin at 12 months (standard treatment group). Measurements of platelet aggregation, high sensitivity CRP and serum and plasma thromboxane are made at the time of recruitment, immediately before the participant stops taking either ticagrelor (Group 2) or aspirin (Group 1). Measurements will also be made at 2, 7 and 14 days after the participants have stopped their medication. This study does not affect patient treatment or their participation in GLOBAL LEADERS in any way.

What are the possible benefits and risks of participating?
The trial's only intervention is phlebotomy. Less than 20ml of blood is being taken. There are no additional adverse risks conferred by participation in the study other than the standard risks carried by phlebotomy. The main benefit of the trial is to participate in developing an understanding of how anti-platelet drugs affect blood clotting. Participation in the trial will not affect the patients' care in any way and patients are not paid for their participation in this trial.

Where is the study run from?
Golden Jubilee National Hospital, Glasgow (UK)

When is the study starting and how long is it expected to run for?
January 2015 to May 2015

Who is funding the study?
NHS National Waiting Times Centre Board (UK)

Who is the main contact?
Mr Michael Campbell

Contact information

Type(s)
Public

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14/WM/1269

Study information

Scientific Title
Is there a rebound increase in platelet aggregation following withdrawal of aspirin or ticagrelor in patients who have recently undergone PCI with DES? An observational study

Acronym
REBOUND

Study objectives
Observational study aiming to evaluate whether there is a rebound increase in platelet aggregation in response to collagen when either ticagrelor or aspirin are withdrawn in patients who have been on dual therapy following percutaneous coronary intervention (PCI).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Nation Research Ethics Approval (UK) , ref: 14/WM/1269

Study design

Single centre, observational cohort substudy of an open label randomised control trial - A GLOBAL LEADERS substudy.

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format

Health condition(s) or problem(s) studied
Effects of dual anti-platelet therapy on platelet aggregation in patients who have received percutaneous coronary intervention (PCI) with coronary stenting.

Interventions
This prospective, single centre, observational study will recruit “all comer” patients enrolled in the GLOBAL LEADERS study who are attending the Clinical Research Facility in the Beardmore Centre for Health Sciences, Golden Jubilee National Hospital immediately before the scheduled discontinuation of DAPT. Patients will be provided with details of the study and consented during their attendance. We anticipate two cohorts of patients: Group 1, previously randomised to change from ticagrelor and aspirin to ticagrelor monotherapy 1 month following PCI; Group 2, previously randomised to switch from ticagrelor and aspirin to aspirin monotherapy at 12 months (standard treatment group). Baseline measurements of platelet aggregation, high sensitivity CRP and serum and plasma thromboxane will be made at the time of recruitment, immediately prior to discontinuation of either ticagrelor (Group 2) or aspirin (Group 1). Measurements will also be made at 2, 7 and 14 days after cessation of DAPT. This study will not effect patient treatment or their participation in GLOBAL LEADERS in any way.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
1. Ticagrelor 2. Aspirin

Primary outcome measure
Platelet aggregation in response to collagen measured using impedance aggregometry. Multiplate©. Measured on DAPT treatment and 2, 7 and 14 days after cessation. Once DAPT has been stopped patients will continue with aspirin or ticagrelor monotherapy according to their randomisation status in GLOBAL LEADERS.

Secondary outcome measures
1. Platelet aggregation in response to arachidonic acid, ADP or thrombin receptor activator peptide 6 (TRAP-6). Measured using impedance aggregometry (Multiplate©).
2. High sensitivity C-Reactive Protein (hsCRP) (using particle enhanced immunonephelometry with Immage analyzer Beckman Coulter)
3. Serum and plasma thromboxane measured using ELISA (R&D Systems Europe; cat. no. KGE011).

All secondary endpoints will be measured on DAPT treatment and 2, 7 and 14 days after cessation.

Overall study start date
12/01/2015

Completion date
19/05/2015

Eligibility

Key inclusion criteria
1. Patients eligible for this study are those already enrolled in the GLOBAL LEADERS study under the care of the Golden Jubilee National Hospital (UK) during the allocated study period.
2. The inclusion criteria for the GLOBAL LEADERS trial will apply to this study including:
2.1. Age ≥18 years
2.2. Presence of one or more coronary artery stenoses of 50% or more in a native coronary artery or in a saphenous venous or arterial bypass conduit suitable for coronary stent implantation
2.3. Able to provide informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Exploratory study, therefore accurate power calculation is difficult. However, based on similarly designed studies, with similar methodologies, it is anticipated around 60 patients will be recruited. (30/group)

Key exclusion criteria
The exclusion criteria for the GLOBAL LEADERS study will also apply to this study including:
1. Known intolerance to aspirin, P2Y12 inhibitors, bivalirudin, stainless steel or biolimus

2. Intake of a strong CYP3A4 inhibitor (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir), as co-administration may lead to a substantial increase in exposure to ticagrelor
3. Moderate to severe hepatic impairment (alanine-aminotransferase ≥ 3 x ULN)
4. Planned surgery, including CABG as a staged procedure (hybrid) within 12 months of the index procedure, unless dual antiplatelet therapy is maintained throughout the peri-surgical period
5. Need for chronic oral anti-coagulation therapy
6. Active major bleeding or major surgery within the last 30 days
7. History of intracranial haemorrhagic stroke or intra-cranial aneurysm
8. Stroke (any type) within the last 30 days
9. Pregnancy at time of randomisation
10. Breastfeeding at time of randomisation
11. Currently participating in another trial and not yet at its primary endpoint

Date of first enrolment
12/01/2015

Date of final enrolment
12/04/2015

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Golden Jubilee National Hospital
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Sponsor information

Organisation
NHS National Waiting Times Centre Board

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/0103jbm17

Funder(s)

Funder type
Government

Funder Name
NHS NWTCB Endowment Funds (UK)

Results and Publications

Publication and dissemination plan

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No