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The effect of ticagrelor monotherapy on platelet reactivity

Submission date 04/02/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/06/2014	**Overall study status** Completed	
Last Edited 14/12/2020	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

A blocked or seriously narrowed coronary artery (that supply the heart) usually causes chest pain during exercise or a heart attack when blood supply to the heart muscle is interrupted. This is commonly treated using Percutaneous Coronary Intervention (PCI). During this treatment, a wire is inserted into the coronary artery, a small balloon is inflated to open up the blockage and a small tube called a coronary stent is left in place to help keep the coronary artery open. Although this is a very effective treatment, there is a risk of new blood clots forming after the PCI and causing another blockage in the coronary artery. For this reason, patients are routinely treated with drugs, such as Clopidogrel and Aspirin. These drugs work by reducing the activity of a type of blood cells, called platelets, which are part of the normal blood clotting process, but also cause abnormal clots in coronary arteries. For many patients who have a coronary stent inserted during a PCI treatment, a 6 to 12 month course of Clopidogrel and Aspirin are given in combination. Aspirin alone is given on its own following the Clopidogrel and Aspirin course. Recently, a new anti-platelet drug called Ticagrelor has been developed that is similar to Clopidogrel, but has a more powerful effect on blood platelets. Ticagrelor in combination with Aspirin is now given to some groups of NHS patients after PCI because a large clinical study has shown that this Ticagrelor with Aspirin is better at preventing abnormal blood clots than Clopidogrel used in combination with Aspirin. Ticagrelor is only routinely used at present in combination with Aspirin. However, Ticagrelor is a powerful anti-platelet drug that almost completely reduces the activity of platelets tested in the laboratory, even without additional Aspirin. This could mean that it is unnecessary to give patients Aspirin as well as Ticagrelor to prevent blood clot formation after coronary stent insertion. This may be beneficial to patients because Aspirin treatment can cause some side effects such as stomach bleeding. This study will identify whether patients who have had a coronary stent inserted also have fully reduced platelet activity during treatment with Ticagrelor. This will be done by measuring the activity of platelets in blood samples using sensitive laboratory tests. The test results from participants taking Ticagrelor alone will then be compared to test results from participants taking Ticagrelor in combination with Aspirin and other combinations of anti-platelet drugs.

Who can participate?

Patients who have had a PCI treatment at the Bristol Heart Institute (UK) with stent insertion for heart disease and have received a course of Clopidogrel and Aspirin

What does the study involve?
Each participant is asked to attend three study visits. Study visit 1 occurs after a course of treatment with Aspirin and Clopidogrel (i.e: at the time dual antiplatelet therapy would be stopped in routine care and participants would have continued indefinitely with daily Aspirin alone). Participants give blood sample 1 for platelet testing. The patient is randomly allocated to one of two different treatment groups. The Aspirin + Ticagrelor group receive Ticagrelor (180 mg) followed by Ticagrelor 90 mg twice a day along with Aspirin once a day for 4 weeks. The Ticagrelor alone group receive a starting dose of Ticagrelor (180 mg) followed by Ticagrelor 90mg twice a day, but no Aspirin for 4 weeks. Study visit 2 is 4 weeks after the study visit 1. All participants give another blood sample for platelet testing. Medication for participants in both groups is then changed to Aspirin 75 mg/day only. Study visit 3 is 4 weeks after the study visit 2. All participants again give a blood sample for platelet testing. Participants then continue on Aspirin only, as usual care.

What are the possible benefits and risks of participating?
The effects of Ticagrelor on platelet function is known when used as a part of a dual anti-platelet treatment with Aspirin and as a single anti-platelet treatment. These results will enable direct comparison of how well these alternative Ticagrelor treatment regimens work and comparison with existing anti-platelet regimens (Aspirin alone and Aspirin+ Clopidogrel). There is no direct benefit to participants, other than the knowledge that they are helping to improve care for all future patients (which may include themselves, friends or family). Apart from the small risks associated with taking blood samples, there is also a risk of side effects to Ticagrelor, the most common being shortness of breath.

When is the study starting and how long is it expected to run for?
The study started in December 2015 and will be completed within 22 months.

Where is the study run from?
University Hospitals Bristol (UHB) (UK)

Who is funding the study?
AstraZeneca's UK Marketing Company (UKMC)

Who is the main contact?
Dr Andrew Mumford
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2013-002734-20

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
v6.0 10/07/2015

Study information

Scientific Title
A randomised controlled trial investigating the pharmacodynamic effect of TicagrElor Monotherapy on PLATElet reactivity in patients with coronary artery disease

Acronym
TEMPLATE

Study objectives
Platelets from patients taking ticagrelor alone and from patients taking aspirin and ticagrelor show similar levels of reactivity defined as the maximum amplitude of the light transmission aggregation response to Thrombin receptor agonist peptide-6 (TRAP).

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford A, 23/10/2014, ref: 14/SC/1309

Study design
Single-centre open-label randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Coronary artery disease and ischaemic heart disease

Interventions
Study visit 1: All participants will give blood sample 1 for platelet testing, receive a loading dose of 180mg ticagrelor, and will be randomised to one of the interventional groups below.
1. Aspirin + ticagrelor (aspirin 75mg/day AND ticagrelor 90 mg b.d. (twice daily)) for 4 weeks, or
2. Ticagrelor (90 mg b.d) for 4 weeks.

Study visit 2: Participants will give blood sample 2 for platelet testing. Medication for participants in both groups will then be changed to aspirin 75 mg/day only.

Study visit 3: All participants will give blood sample 3 for platelet testing. Participants will then continue on aspirin only, as per standard care (usually under the supervision of their GP).

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Maximum amplitude of the light transmission aggregation response of platelet rich plasma (PRP) to 10 μM TRAP expressed as a % of the absolute difference in light transmission between PRP and platelet poor plasma. This assay measures the ability of platelets to aggregate when exposed to the aggregation promoting agent TRAP.

Measured at each visit, i.e. at visit 1 (baseline visit), at visit 2 (4 weeks after the baseline visit), and at visit 3 (8 weeks after the baseline visit).

Secondary outcome measures
1. Light transmission aggregation responses to collagen and to ADP, arachidonic acid and the thromboxane (TP) receptor agonist U46619. This assay measures the ability of platelets to aggregate when exposed to the aggregation promoting agents collagen, ADP, arachidonic acid and U46619.
2. Flow cytometry to quantify surface CD62P expression and PAC-1 binding before and after activation with collagen and TRAP6. This assay measures the exposure of surface activation markers.
3. Plasma concentrations of soluble CD40 ligand (sCD40L) and thromboxane B2 to assess baseline in vivo platelet activation and Thromboxane A2 (TxA2) bio-synthesis respectively. This assay measures the levels of chemicals in the blood that are released when a platelet is activated and reflects the extent of platelet activation in the circulation.

Measured at each visit, i.e. at visit 1 (baseline visit), at visit 2 (4 weeks after the baseline visit), and at visit 3 (8 weeks after the baseline visit).

Overall study start date
14/12/2016

Completion date
14/12/2018

Eligibility

Key inclusion criteria
1. Patient is treated with dual antiplatelet therapy comprising aspirin and clopidogrel for a minimum of 4 weeks (amended from: for 12 months as of 31/03/2016)
2. The patient is scheduled to stop dual antiplatelet therapy and continue with aspirin monotherapy

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
110

Total final enrolment
110

Key exclusion criteria
1. Contraindication to dual antiplatelet therapy
2. Interruption of dual antiplatelet therapy because of bleeding events or increased bleeding risk
3. Contraindications to the use of ticagrelor
4. Pregnant and or lactating women
5. Women with child bearing potential (i.e. not sterilised or not post-menopausal) who are unwilling to use contraception
6. Men with a spouse or partner with child bearing potential unless the participant has agreed to use condoms

Date of first enrolment
15/01/2016

Date of final enrolment
15/10/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Bristol
Bristol
United Kingdom
BS2 8HW

Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Protocol paper: 2016
2. Results paper: 2018

Intention to publish date
31/12/2016

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?
Protocol article	protocol	09/11/2017		Yes	No
Results article	results	15/12/2020	14/12/2020	Yes	No
HRA research summary			28/06/2023	No	No