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# The effect of ticagrelor monotherapy on platelet reactivity

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

### Contact details
University of Bristol
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# Additional identifiers

### Clinical Trials Information System (CTIS)
2013-002734-20

### Protocol serial number
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

### Study type(s)
Treatment

### 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(s)
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).

### Key secondary outcome(s))
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).

### 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

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
All

### 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
United Kingdom

England

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

## Sponsor information

**Organisation**
University Hospitals Bristol NHS Foundation Trust

**ROR**
https://ror.org/04nm1cv11

# Funder(s)

**Funder type**
Industry

**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**

**IPD sharing plan summary**
Available on request

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 15/12/2020 | 14/12/2020 | Yes | No |
| Protocol article | protocol | 09/11/2017 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |