

Influence of treatment adherence to clopidogrel on platelet aggregation in subjects carrying coronary stent

Submission date 31/08/2010	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 14/01/2011	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 15/10/2020	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Michel Burnier

Contact details
Head of the Division of Nephrology and Hypertension
Centre Hospitalier Universitaire Vaudois
Rue du Bugnon 17
Lausanne
Switzerland
1011
+41 (0)21 314 11 29
michel.burnier@chuv.ch

Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

Influence of treatment adhesion to clopidogrel on platelet aggregation in subjects carrying coronary stent: an interventional single centre randomised double-blinded open label trial with three parallel arms

Acronym

Eurostar

Study objectives

The analysis of therapeutic adhesion finds a particularly interesting application in the specific case of clopidogrel, an anti-platelet drug, cornerstone in association with aspirin in the treatment of patients undergoing percutaneous coronary interventions. However, the evidence that some patients persist with enhanced platelet reactivity despite treatment with clopidogrel suggest that individual responsiveness to clopidogrel is not uniform and is subject to inter- and intra-individual variability.

Notably, there is a growing degree of evidence that a poor biological response to clopidogrel is associated with the recurrence of cardiovascular ischaemic events. Therefore, the identification of patients "non-responders" constitutes a major therapeutic challenge. To prove lack of efficacy of clopidogrel in a particular patient, we must previously ensure that the drug was administered correctly by answering a key question: Is the patient really a "non-responder" or rather a "non-adherent" to treatment?

The monitoring of treatment adhesion by an electronic control device called MEMS® (Medication Event Monitoring System; AARDEX, Zug, Switzerland) is presently considered the most accurate and sensitive approach to get full information on drug intake. The MEMS® consists in a usual bulk pill container fitted with a special cap, which contains a microelectronic system that automatically records the date and hour of each opening of the bottle.

For therapeutic study purpose, the MEMS® can be utilised in an "usual care" setting (blinding of investigator, physician and patient for adhesion results) or in a classical "integrated care" setting (regular individual drug adhesion results reporting and discussion).

Several methods have been used to assess in vitro clopidogrel-induced anti-platelet effects. Flow cytometric assessment of VASP-P (VASP assay) is a marker of P2Y₁₂ receptor reactivity, thus specific of clopidogrel-induced inhibition. A reduced P2Y₁₂ reactivity ratio is indicative of more enhanced clopidogrel-induced inhibition.

Ethics approval required

Old ethics approval format

Ethics approval(s)

This study was presented to the Commission cantonale (VD) d'éthique de la recherche sur l'être humain in Switzerland, and approved on the 12th March 2010 (ref: 56/10 EUROSTAR)

Study design

Interventional single centre randomised double-blinded open label trial with three parallel arms

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Coronary stenting

Interventions

Group 1: standard care 6 month follow-up, without electronic pillbox. Total visits: 3.

Group 2: 6 months follow-up with double blinded electronic pillbox (MEMS®), usual care, without feed-back on adherence results. Total visits: 3.

Group 3: 6 months follow up with electronic pillbox (MEMS®), integrated care, with motivational feed-back on adherence results. Total visits: 5.

For each group, a follow-up of the cardiologic events will be made at 12, 24 and 36 months by phone.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Clopidogrel

Primary outcome(s)

Platelets aggregation (determined by the VASP assay, as index of platelet reactivity) at 6 months

Key secondary outcome(s)

1. Incidence of cardiovascular events, including: acute non-lethal myocardial infarction, stent thrombosis, cardiovascular mortality
2. Incidence of hemorrhagic complications
3. Drug adherence to clopidogrel using the MEMS® on a 6 months period. The adherence will be measured by 4 parameters: percentage of doses taken, taking adherence, percentage of drug holidays, persistence.
4. Influence of the CYP2C19 polymorphism on aggregation studies in the long term follow-up of patients after coronary stent implantation

Completion date

01/10/2015

Eligibility

Key inclusion criteria

1. Adult patients greater than 18 years, either sex
2. Treated with clopidogrel (Plavix®) for greater than 6 months after coronary stent implantation (indication: stable/unstable angina or non-invasive functional test positive for myocardial ischaemia) in the interventional cardiology department

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

120

Key exclusion criteria

1. Heart failure classification according to New York Heart Association (NYHA) class III or IV
2. ST and non-ST elevation myocardial infarction (less than 1 month)
3. Platelets less than 100,000/l
4. Inflammatory diseases requiring prednisone treatment
5. Medical history of:
 - 5.1. Acute or chronic thrombocytopenia
 - 5.2. Ticlopidine allergy
 - 5.3. Active gastric ulcer (less than 2 months)
 - 5.4. Cerebral hemorrhage (less than 6 months)
 - 5.5. Uncontrolled hypertension greater than or equal to 180/110 mmHg
 - 5.6. Liver Insufficiency CHILD-score greater than or equal to 1
 - 5.7. Bleeding diathesis
 - 5.8. Pregnancy, breast feeding
 - 5.9. Associated drug therapy with CYP2C19 inhibitors

Date of first enrolment

01/04/2010

Date of final enrolment

01/10/2015

Locations**Countries of recruitment**

Switzerland

Study participating centre

Head of the Division of Nephrology and Hypertension

Lausanne

Switzerland

1011

Sponsor information

Organisation

University Hospital Centre and University of Lausanne (CHUV) (Switzerland)

ROR

<https://ror.org/05a353079>

Funder(s)

Funder type

Government

Funder Name

Swiss Federal Office of Training and Technology (OFFT) (Switzerland) (ref: Eurostar project no. 4776; OFFT contract no: INT.2009.0026)

Funder Name

EUROSTAR Consortium (a consortium of international partners funds the European project):

Funder Name

ABR Pharma (France)

Funder Name

Citobi (Belgium)

Funder Name

Pharmionic Systems Ltd (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	25/10/2017	15/10/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes