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

Submission date 31/08/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/01/2011	**Overall study status** Completed	
Last Edited 15/10/2020	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

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 below to request a patient information sheet

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

Secondary outcome measures
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

Overall study start date
01/04/2010

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Total 225 patients: Group 1: n = 90, Group 2 : n = 45, Group 3: n = 90

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
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Sponsor information

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

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Sponsor type
Hospital/treatment centre

Website
http://www.chuv.ch/

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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