ISRCTN64082539 https://doi.org/10.1186/ISRCTN64082539

Antiplatelet therapy tailoring after primary percutaneous coronary intervention (PCI)

Submission date	Recruitment status	[ ] Prospectively registered
08/02/2010	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
18/02/2010	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
18/02/2010	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Igor Mrdovic

Contact details
Pasterova 2
Beograd
Serbia
11000
+38 (0)11 6346 2488
igormrd@gmail.com

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
553/12

Study information

Scientific Title
Antiplatelet Regimen Tailoring after primary Percutaneous Coronary Intervention (ART-PCI): a single centre longitudinal cohort prospective trial

Acronym
ART-PCI

Study objectives
Assessment of platelet residual aggregation (APRA) may help to identify patients at increased risk for major thrombotic events after primary percutaneous coronary intervention (pPCI), who may benefit from antiplatelet regimen tailoring (ART).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Clinical Center of Serbia approved on the 2nd June 2009 (ref: 553/12)

Study design
Single centre observational longitudinal cohort prospective trial

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Quality of life

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
ST-elevation myocardial infarction (STEMI)

Interventions
Multiple electrode aggregometry (MEA) is performed using an impedance aggregometer (Multiplate analyzer, Dynabyte GmbH, Munich, Germany). Whole blood is sampled 24 hours after the procedure and placed in 7 ml plastic tubes containing the anticoagulant heparin (50 U/ml). For patients who received IIb/IIIa inhibitor tirofiban, blood samples are obtained at least 24 hours after the completition of tirofiban infusion. Blood samples are stored on the room temperature for 30 minutes, diluted (1:2) with 0.9% NaCl solution and incubated on 37 +/- 0.5 °C for 3 minutes, using a computer-controlled electronic pipette.

ASPI test is used to detect the effect of aspirin using the ciclooxygenase substrate arachidonic acid (final concentration 0.5 mM/L). ADP test is used to assess the blockade of ADP receptor by

clopidogrel. Aggregation is continuously recorded for 6 minutes after ADP (final concentration 6.4 gM/L) is added. PGE1, as a suppressor of intracellular free calcium, is simultaneously added to increase the test's sensitivity to ADP. The increase of impedance is transformed to aggregation units (AU) that are plotted against time as area under the curve (AU/min). TRAP test resembles direct activation of the thrombin receptor using the thrombin receptor activating peptide (final concentration 32 gM/L).

PRA above 50%, compared to the basal value estimated by TRAP test, is linked with low responding (LR) to clopidogrel. A 150 mg daily clopidogrel is instituted in low-responders (LRs) during the first 30 days after the procedure. The second APRA is obtained 7 days after the first test. In LRs, the 500 mg maintenance dose of ticlopidine is administrated instead of clopidogrel. A 300 mg aspirin daily is administrated during the next 30 days to all patients without contraindications. After 30 days, the doses will be reduced to 100 mg aspirin and 75 mg clopidogrel.

Patients will be followed-up at 30 days and 1 year after enrolment by telephone interviews and /or outpatient visits. Interviewers will be blinded to the results of platelet aggregation. An independent Clinical Event Committee will adjudicate the occurrence of the major events and major bleeding. Safety data will be reviewed monthly by an independent Safety Monitoring Committee. Statistical analyses will be performed by the Institute for Medical Statistics and Informatics, School of Medicine, Belgrade, Serbia.

Statistical analysis:
Continuous variables are expressed as median values with 25th and 75th quartiles, whereas categorical variables are expressed as frequency and percentage. Analysis for normality of data are performed using the Kolmogorov-Smirnov test. Baseline differences between groups are analysed using the independent Student t-test or Mann-Whitney test for continuous variables, and Pearson X2 test for categorical variables. Univariable logistic regression model is used to identify risk factors influencing clinical outcomes at 30-day follow-up. Time-to-event outcomes are presented using Kaplan-Meier curves; differences between groups are compared using a 2-sided log-rank test. Multivariate logistic regression analysis will be performed to identify independent predictors of high PRA as dependent variables. Variables are selected by backward method with a P-value of less than 0.1 as entry criterion. The cut-off values for significant predictors are determined using receiver operating characteristic (ROC) analysis.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Efficacy outcome:
Major adverse cardiovascular events (MACE). MACE comprises death, nonfatal reinfarction, ischaemic stroke and target vessel revascularisation (TVR). Nonfatal reinfarction is defined as the presence of at least two of the three following criteria:
1. Recurrent ischaemic chest pain longer than 20 minutes
2. Reoccurrence of ST elevation greater than 0.1 mV or new pathognomonic Q waves in at least two contiguous leads, and
3. Increase of cardiac troponin over the upper reference limit (URL) and over 50% of the lowest recovery level from the index myocardial infaction (MI)

The more than triple URL value of cardiac troponin after PCI is defined as PCI-related myocardial infarction. Stroke is defined as a new onset of focal or global neurological deficit lasting more than 24 hours, and is computed tomography (CT)-classified as ischaemic. Haemorrhagic stroke is counted as life-threatening bleeding and is not included into stroke analyses. Target-vessel revascularisation is defined as ischaemia-driven revascularisation of the infarction-related artery during the follow-up period.

Safety outcome:
Major bleeding. Bleeding events were classified according to Thrombolysis In Myocardial Infarction (TIMI) criteria.

All primary and secondary endpoints will be recorded at 1 month and at 1 year after the enrolment.

Secondary outcome measures
Subacute stent thrombosis. All primary and secondary endpoints will be recorded at 1 month and at 1 year after the enrolment.

Overall study start date
01/06/2008

Completion date
28/02/2010

Eligibility

Key inclusion criteria
1. ST-elevation myocardial infection (STEMI) patients undergoing primary PCI in our institution
2. Both genders, aged greater than 18 years
3. Platelet residual aggregation (PRA) assessed 24 hours after the loading with clopidogrel 600 mg
4. Control group: 1000 patients enrolled in the RISK-PCI trial (see http://www.controlled-trials.com/ISRCTN83474650) in our centre from February 1st, 2006 till June 1st, 2008, who did not have platelet function assays

Low responders to clopidogrel will be subjected to ART if there is no exclusion criteria for ART.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

700 patients in the ART group and 1000 patients in the control group

Key exclusion criteria
1. Not alive until 24 hours from clopidogrel loading 600 mg
2. Aged greater than 75 years
3. Percutaneous balloon angioplasty (POBA) without stenting
4. Failed pPCI
5. Active bleeding in hospital
6. Coronary dissection with pericardial collection
7. Haemoglobin (Hb) less than 80 g/dL needing transfusion in hospital
8. Simultaneous treatment with oral anticoagulants
9. Candidates for urgent bypass surgery
10. Low basal thrombin receptor activating peptide (TRAP) value (less than 500 AU/minute)
11. Hystory of recent bleeding from ulcer
12. Thrombocyte count less than 100,000/ml
13. Drug non-compliance
14. Withdrawal of consent

Date of first enrolment
01/06/2008

Date of final enrolment
28/02/2010

Locations

Countries of recruitment
Serbia

Study participating centre
Pasterova 2
Beograd
Serbia
11000

Sponsor information

Organisation
Clinical Centre of Serbia (Serbia)

Sponsor details
Pasterova 2
Beograd
Serbia
11000

+38 (0)11 1361 8444
cdcc@klinicki-centar.rs

Sponsor type
Hospital/treatment centre

Website
http://www.klinicki-centar.rs

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Clinical Centre of Serbia (Serbia)

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