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Non-Interventional Study (NIS) Report

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Observational Prospective study to esTIMAte the rates of outcomes in patients undergoing PCI with drug eluting stent (DES) implantation who take statins (OPTIMA)

Study dates:	**First Subject In: 21/12/2009** **Last Subject Last Visit: 26/12/2011**

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NIS REPORT SYNOPSIS

Observational Prospective study to esTIMAte the rates of outcomes in patients undergoing PCI with drug eluting stent (DES) implantation who take statins (OPTIMA)

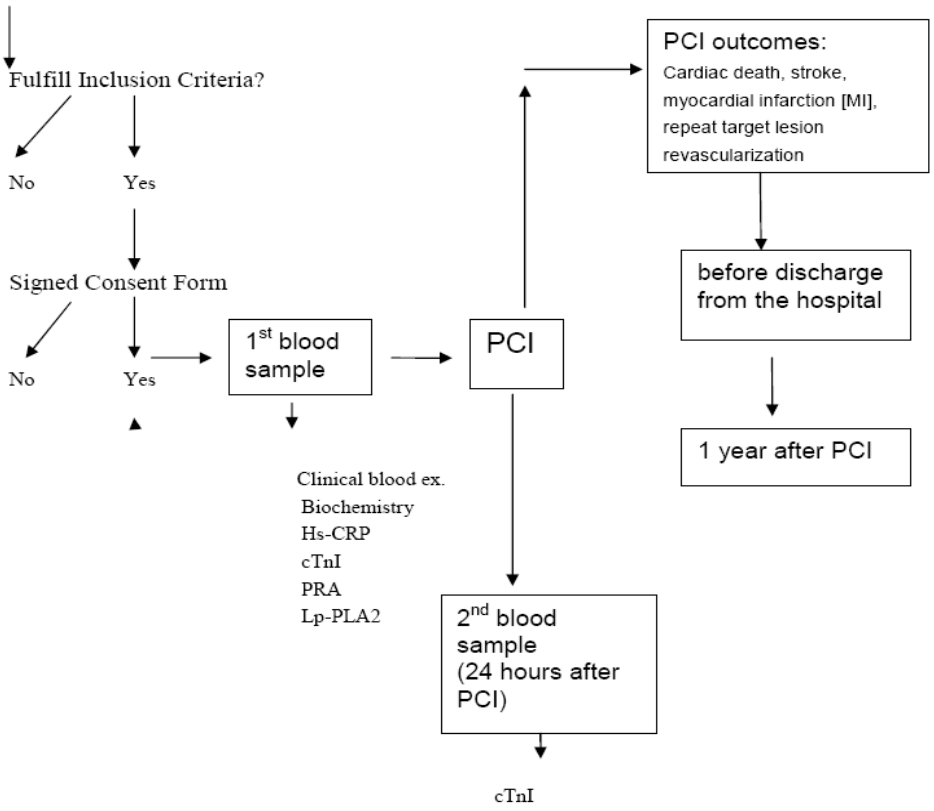
Study Sites

The study was conducted in the Russian Federation. 1 site participated in the study and 602 patients with stable angina and indication to PCI were enrolled. No investigational drug was used in this study. All patients received treatment in accordance with routine clinical practice in the study site. The sample size calculation was performed with the aim to obtain estimates of adverse outcome rate with a 95% confidence interval of no more that +/- 5% around the point estimates. For the descriptive analysis, 600 patients allow to estimate an expected proportion of 0.07 – 0.2 with a precision of 0.02 - 0.032, which means, for example, estimating 20% with a confidence interval from 16.8% to 23.2% (α=0.05).

Study design

Overall study design and flow chart

This was an observational prospective study based on the data collected during 3 visits: before and after PCI performed at the Russian Cardiological Research Complex (РКНПК). From the date of the study start and until the end of the study physicians enrolled hospitalized patients with stable angina undergoing elective PCI and who met appropriate inclusion criteria.



Inclusion Criteria

For inclusion in the study subjects were to fulfil all of the following criteria:

1. Stable angina with indication to PCI
2. Hospitalization to Russian Cardiological Research Complex (РКНПК) for PCI procedure with drug-eluting stents implantation
3. Statin therapy initiated for at least one month prior to PCI
4. Written informed consent provided prior the start of participation in the study.

Exclusion Criteria

1. Subjects who are unwilling or unable to provide informed consent.
2. Presence of ACS during the current hospitalization
3. Severe CHF (NYHA III/IV) or LVEF<40 %
4. Stroke within 6 months before PCI
5. Acute or chronic inflammatory disease
6. Anti-inflammatory medications intake, with the exception of aspirin
7. Severe liver or muscle disease
8. Severe kidney disease / renal failure with creatinine > 3 mg/dl
9. History of oncologic disease
10. Conceivable impossibility to come in touch with the patient or his family at 1-year after the intervention.

Criteria for Early Discontinuation

Patients may be discontinued from study assessments at any time. Specific reason for discontinuing a patient from this study is:
Voluntary early discontinuation by the patient who is at any time free to discontinue his/her participation in the study, without prejudice to further treatment.

Procedures for discontinuation

Patients who discontinue were to be asked be asked about the reason(s) for their discontinuation.

Criteria For Evaluation (Main Variables)

The following variables were measured in this study:
• Demographic patient characteristics: age, gender, social status
• Smoking, alcohol consumption
• Relevant medical history: family history of CAD, including premature CAD in close relatives (male<55 years, female <65 years; cardiovascular diseases: atherosclerosis, angina, CHF, primary and secondary hypertension; rhythm disturbances, heart valvular disease, cardiac myopathy, date of CVD diagnosis, previous coronary revascularizations (e.g. PCI or CABG).
• History of atherosclerosis (cerebral atherosclerosis, atherosclerosis of lower extremities, etc.). History of transient ischemic cerebral attack or stroke, history of myocardial
infarction, history of atrial fibrillation.
• Hypercholesterolemia presence, lipid-lowering therapy received by patient for at least one month before inclusion in the present study (medications, daily doses, date of initiation and duration of therapy).
• Other significant concomitant diseases (diabetes mellitus, peptic ulcer, abdominal pain and liver impairment, etc.).
• Concomitant therapy: antihypertensives, aspirin, oral antidiabetics, insulin, clopidogrel, beta-adrenergic blockers, ACE inhibitors, proton pump inhibitors and other drug therapy (the trade names of medications, daily doses, route of administration, date of initiation
and duration of therapy).
• Physical examination data (body weight, height, systolic and diastolic blood pressure, heart rate, pulse regularity/heart rhythm).
• Admission diagnosis (Stable Angina Pectoris severity (e.g. class I-II or class III-IV), mild to moderate CHF (NYHA I/II), etc.
• Laboratory assessment data (clinical blood examination, biochemistry, aldosterone, inflammatory and cardiac markers, plasma renin activity).
• Procedural factors: LVEF, characteristics of the vessel lesion type (multivessel CAD, type C lesion, type B lesion, intracoronary thrombosis in other segments), number of stents per patient, total stent length and stent diameter.
• Major adverse cardiac and cerebrovascular events (MACCE) composite of cardiac death, stroke, myocardial infarction [MI] and repeat target lesion revascularization.
• Stent thrombosis according to ARC classification.

All the patient's data, medical history and therapy were documented in hospital records. Information needed for CRF entering was recorded based on patient's medical source

document data.

Primary variable

Primary variable in this study is Major adverse cardiac and cerebrovascular events (MACCE) - composite of cardiac death, stroke, myocardial infarction [MI] and repeat target lesion revascularization.

Other variables

• Early and late stent thrombosis
• Low Density Lipoprotein Cholesterol (LDL-C) levels prior to PCI
• Inflammatory markers level (C-reactive protein (CRP) and Leukocytes) in patients prior to PCI
• Cardiac marker Troponin I level prior and after PCI, plasma renin activity (PRA) and aldosterone level in patients before PCI
• Lipoprotein associated phospholipase A2 level (Lp PLA2) in patients before PCI
• Demographic patient characteristics: age, gender, social status
• Smoking, alcohol consumption
• Relevant medical history: family history of CAD, including premature CAD in close relatives (male<55 years, female <65 years; cardiovascular diseases: atherosclerosis, angina, CHF, primary and secondary hypertension; rhythm disturbances, heart valvular disease, cardiac myopathy, date of CVD diagnosis, previous coronary revascularization (e.g. PCI or CABG).
• History of atherosclerosis (cerebral atherosclerosis, atherosclerosis of lower extremities, etc.). History of transient ischemic cerebral attack or stroke, history of myocardial
infarction.
• Hypercholesterolemia presence, lipid-lowering therapy received by patient for at least one month before inclusion in the present study (medications, daily doses, date of initiation and duration of therapy). The rates of lipid target level achievement.
• Other significant concomitant diseases (diabetes mellitus, peptic ulcer, abdominal pain, and liver impairment, etc.)
• Concomitant therapy: antihypertensives, aspirin, oral antidiabetics, insulin, clopidogrel, beta-adrenergic blockers, ACE inhibitors, proton pump inhibitors and other drug therapy (the trade names of medications, daily doses, route of administration, date of initiation
and duration of therapy).
• Physical examination data (body weight, height, systolic and diastolic blood pressure, pulse rate, pulse regularity).
• Admission diagnosis (Stable Angina Pectoris functional class (e.g. class I-II or class III-IV) mild to moderate CHF (NYHA I/II),etc.
• Procedural factors: LVEF, characteristics of the vessel lesion type (multivessel CAD, type C lesion, type B lesion, intracoronary thrombosis in other segments), number of stents per patient, total stent length and stent diameter.

Statistical analysis methods

All included into the study patients (602) met Inclusion/Exclusion criteria (had stable angina with indication to PCI, were admitted to Russian Cardiological Research Complex for PCI

procedure with drug-eluting stents implantation, took statin therapy for at least one month prior to PCI, provided written informed consent, had no any exclusion criterion.

Disposition of Patients

The following disposition summaries were provided as separate tables:

- A summary of the number of patients screened (Population: All Patients);
- A summary of the number of patients and the number and percentage of patients completing Visit 2 and Visit 3 of the study (Population: All Patients);
- A summary of the number and percentage of patients violated inclusion/exclusion criteria (Population: All Patients);
- A summary of the number and percentage of early withdrawals by major reason and overall. (Population: All Patients).

Analysis Populations

The following populations were defined:

- All Patients: All patients who were screened into the study and have started the CRF.
- Early Outcome set: All eligible patients who underwent PCI procedure with drug – eluting stents implantation and provided baseline and early outcome data at Visit 2. This population used for the descriptive and early outcome analyses.

  Late Outcome set: All eligible patients underwent PCI procedure with drug –eluting stents implantation and provided baseline and late outcome data at Visit 3. This population used for the descriptive (Visit 3 data) and late outcome analyses

SUMMARY

The primary objective of this study is to estimate the rates of percutaneous coronary intervention (PCI) outcomes in patients after drug-eluting stents implantation who take statins.

The proportion of patients with Major Adverse Cardiac and Cerebrovascular Event (MACCE) at Visit 2 (Early outcomes) was estimated as 10.6% (95%CI - 8,2%; 13,1%).

The proportion of patients with MACCE assessed at Visit 3 (Late outcomes) was estimated as 9,5% (95%CI - 7,13%; 11,86%).

Different prognostic factors and their association with PCI (MACCE) outcomes were evaluated in patients undergoing PCI with drug eluting stent (DES) implantation who take statins.

The following factors have shown p-value below significance level (0.05) in the univariate analysis of early PCI outcomes: erythrocytes sedimentation reaction ESR ($p=0.003$); total stent length ($p<0.001$); number of stents per patient ($p=0.004$); CX stenting ($p=0.043$), type C injury ($p=0.039$); bifurcational stenting ($p<0.001$); Percutaneous Transluminal Coronary Angioplasty (PTCA) in the other segments ($p=0.001$); paclitaxel stent cover ($p=0.025$); occlusion intervention ($p=0.018$).

The following factors have shown p-value below significance level (0.05) in the multivariate analysis of early PCI outcomes: ESR (p=0.01) and total stent length (p=0.002).

The following factors have shown p-value below significance level (0.05) in the univariate analysis of late PCI outcomes: age (p=0.026); C-reactive protein CRP (p<0.001); ESR (p=0.043); PTCA in the other segments (p=0.051); venous bypass intervention (p=0.002) and everolimus stent cover (p=0.048).

The following factors have shown p-value below significance level (0.05) in the mulivariate analysis of late PCI outcomes: CRP (p=0.01); ESR (p=0.011) and venous bypass intervention (p=0.004).

Low Density Lipoprotein Cholesterol (LDL-C) target level achievement was estimated and lipid-lowering therapy details in patients taking standard lipid lowering therapy prior the PCI was studied.

LDL-C target level was achieved in 141 (23.5 %) patients.

Lipid-lowering therapy in patients prior the PCI included the following statins:

120 (19.9%) patients were taking simvastatin with mean daily dose 16.5mg (10.0 to 40.0, median 20) , intake ongoing in 115 (95.8%) patients.

398 (66.1%) patients were taking atorvastatin with mean daily dose 16.7mg (2.0 to 40.0, median 20) , intake ongoing in 396 (99.5%) patients.

83 (13.8%) patients were taking rozuvastatin with mean daily dose 11.99mg (5.0 to 40.0, median 10) , intake ongoing in 82 (98.8%) patients.

3(0.5%) patients were taking fluvastatin with mean daily dose 60.0mg (20.0 to 80.0, median 80) , intake ongoing in 2 (66.7%) patients.

No patients received Pravastatin.

Inflammatory markers, C-reactive protein (CRP) and white blood cell count, were estimated in patients before PCI.

The mean CRP in patients before PCI was 0.348 (SD 0.564) with median 0.175.

The mean white blood cell count in patients before PCI was 7.00 (SD 1,830) with median 6.8.

Cardiac marker Troponin I, plasma renin activity (PRA) and aldosterone were estimated in patients prior to PCI

The mean Troponin I assessed at a baseline was 0.0138 (SD 0.059) with median 0.1 The mean Troponin I assessed at 24 hours after PCI was 0.542 (SD 1.43) with median 0.1.

The mean plasma renin activity (PRA) in patients before PCI was 2.83127 (SD 5.69) with median 0.8.

The mean aldosterone in patients before PCI was 130.73 (SD 207.20) with median 78.50.

Lipoprotein associated phospholipase A2 (Lp PLA2) in patients before PCI was studied

The mean Lp PLA2 A2 in patients before PCI was 165.62 (SD 70.14) with median 150.00.

Early and late stent thrombosis according to ARC classification were studied.

The frequency of Stent thrombosis at visit 2 was 1% (6 patients).

The Stent thrombosis was acute in 3 (50%)and subacute in 3 (50%) patients.

The frequency of Stent thrombosis at visit 3 (Late outcome) was 1% (6 patients).

Thereby, the study met their objectives.