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CEPHEUS II

CEntralized Pan-Russian survey of tHE Undertreatment of hypercholeSterolemia II

Study dates:	**First Subject In: 09/09/2014** **Last Subject Last Visit: 29/11/2015**

National Coordinating Investigator:

MD MC:

Study Delivery Leader:

NIS REPORT SYNOPSIS

CEPHEUS II

CEntralized Pan-Russian survey of tHE Undertreatment of hypercholeSterolemia II

STUDY SITES

80 clinical sites located in different regions of Russian Federation were included in the study; patients were enrolled in 77 sites.

STUDY DATES

First Subject In: 09 Sep 2014.

Last Subject Last Visit: 29 Nov 2015.

STUDY OBJECTIVES

Primary objective was to determine the proportion of patients at moderate to very high CV risk on lipid-lowering drug therapy who reach the LDL-C goals established by the Fifth Joint European Task Force guidelines (2012).

Secondary objectives were:

1. To determine the proportion of patients at moderate to very high CV risk on lipid-lowering drug therapy who reach the LDL-C goals per the Fifth Joint European Task Force guidelines (2012) in the following sub-populations:

    - Primary prevention patients
    - Secondary prevention patients

2. To identify determinants (e.g., patient and physician characteristics, the type of lipid-lowering agent) for not reaching the LDL-C goals.

3. To identify the percentage of incorrect CV-risk assessments by physicians.

4. To determine the proportion of patients in a subgroup of those with diabetes mellitus (and interpretable HbA1c results who achieve HbA1c standardized[i] target of <7% (per DCCT[1]).

STUDY DESIGN

This was a multi-center survey of patients who were currently receiving lipid-lowering medications and had a moderate or higher CV risk. The survey was conducted in the Russian Federation.

Data collection for each study subject was done within one physician visit. If an enrolled subject came to the visit not fasting (for at least 8 hours), an appointment for the blood tests was to be made for another day.

Prior to the assessment of the first subject at a site, each investigator was to complete an investigator questionnaire on his/her experience and perception of the management of hypercholesterolemia in his/her patients.

Prior to the assessment, subjects were to record on a patient questionnaire their awareness of hypercholesterolemia, their current treatment schedule, their perception, and compliance.

The investigator was to complete a Case Report Form (CRF) with the subject's demographics, known cardiovascular risk factors, cardiovascular medical history, current lipid-lowering drug therapy, and the reason for this therapy.

Fasting blood samples were to be taken in tubes to test for total cholesterol, LDL-cholesterol, HDL-cholesterol, glucose, creatinine, hemoglobin A1c, hemoglobin, and hematocrit at a central laboratory in the Russian Federation.

TARGET PATIENT POPULATION

The patients had to fulfil all of the following criteria:

1. Properly obtained written informed consent from the potential subject

2.18 years of age or older of either gender and any race

3. On lipid-lowering drug therapy for at least 3 months (90 days), with no dose change for a minimum of 8 weeks (56 days)

4. Scheduled blood tests for TC, HDL-C, LDL-C, glucose, creatinine, HbA1c, Hb, and hematocrit on the visit when they were considered for survey participation, or these tests had to be decided to be necessary for study-unrelated purposes during that visit

STUDY VARIABLES

Primary variable was the proportion of patients who reached the LDL-C goals established by the Fifth Joint European Task Force guidelines (2012).

Other variables were:

a) the proportion of patients at moderate to very high CV risk on lipid-lowering drug therapy who reached the LDL-C goals per the Fifth Joint European Task Force guidelines in the following sub-populations:

   - Primary prevention patients,

   - Secondary prevention patients

b) the percentage of incorrect CV-risk assessments made by physicians

c) the proportion of subjects in a subgroup of those with diabetes mellitus and interpretable HbA1c results who achieved HbA1c standardized target of 7% (per DCCT[1]).

Other secondary variables were qualitative. In order to evaluate the association between achievement of the LDL-C goals and patient characteristics, the multivariate logistic regression model was developed. A binary categorical attribute - LDL-C within/outside of the LDL-C target range per the guidelines of the Fifth Joint European Task Force - served as a dependable variable in this model.

STUDY RESULTS

This non-interventional study was a multi-centre survey of patients who are currently receiving lipid-lowering medications and have a moderate or higher CV risk. 2704 patients' data from 77 centres in Russian Federation were analysed in this study. The mean age of patients was 62.73 (±10.01), more than half of patients (56.6%) were between 55 and 69 years. Most of the patients had cardiovascular diseases and risk factors in anamnesis, 91.2% of patients belonged to very high CV risk category. All patients were on lipid-lowering treatment, 99.7% of patients received statins as a monotherapy or in combination with other agents.

Primary objective of this study was to determine the proportion of patients who reached the LDL-C goals established by the Fifth Joint European Task Force guidelines (2012). Secondary objectives were to determine the percentage of responders in sub-populations of primary and secondary prevention patients; to identify determinants for reaching the LDL-C goals; to identify the percentage of incorrect CV-risk assessments by physicians and to determine the proportion of patients with diabetes mellitus who achieved HbA1c target level of <7%.

- The results of this study showed that only 17.4% of study population achieved LCL-C goals established by the Fifth Joint European Task Force guidelines. Along with that in more than half of non-responders with very high cardiovascular risk (55.0%) the

difference between the patient's LDL-cholesterol and target levels and goal didn't' exceed 1 mmol/l.

- The subgroup of primary prevention patients demonstrated significantly higher achievement rate of LDL-C goals (19.7%) in comparison with secondary prevention patients (16.1%).

- Logistic regression analysis showed that probability of the LDL-C goals achievement is lower in patients with family history of early CHD; patients suffered from ischemic heart disease, patients with non-compliance with hypercholesterolemia treatment; patients who are dissatisfied or concerned with the effectiveness of lipid-lowering therapy. Investigators related determinants did not show impact on achievement of the LDL-C target level.

- Overall, in 21.3% of patients discordant estimations of cardiovascular risk between investigators and control assessment were revealed. In most cases, underestimation of CV risk by investigators was registered (in 19.4% of patients); overestimation of risk by investigators was found in 1.9% of patients only.

- More than half (61.9%)of patients with diabetes mellitus and interpretable HbA1c results achieved HbA1c target level of <7% according to results of this survey.

Thus, the result of this non-interventional study demonstrated that despite of the lipid-lowering treatment with statins a significant number is still not reaching the LDL-C goals established by the Fifth Joint European Task Force guidelines. The one from plausible reasons may be due to the underestimation of cardiovascular risk by physicians and as a consequence, insufficient or inadequate dosage of lipid-lowering medications. The obtained results are in line with results of other similar projects including large-scale EUROASPIRE IV study. This study was conducted in 79 centres from 24 European countries during May 2012 to April 2013 [47, 48], only 19.3% of enrolled CHD patients achieved target values of LDL-C < 1.8 mmol/L at the time of interview.