STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Crestor
ACTIVE INGREDIENT: Rosuvastatin

Study No: NIS-CKR-DUM-2008/5

Investigation into the CorrelAtion of pLasma hs-CRP concentrations and cardiovascuLar rISk in Korean populaTiOn (CALLISTO study)

Developmental phase: Marketed
Study Completion Date: 2009-06-30
Date of Report: 2009-09-17

OBJECTIVES:

The primary objective was to evaluate hs-CRP levels according to risk categories by the NCEP ATP III. The secondary objective was to evaluate a relationship between hs-CRP and each CHD CVD risk factor including LDL-C.

METHODS:

The following information was collected in this study by a retrospective chart review: basic items including sex, age, clinic visit date, presence or absence of metabolic syndrome, LDL-C goal levels, latest lipid levels, CRP levels, HbA1C, and concurrent drugs. For risk factors, cigarette smoking, hypertension, and diabetes were confirmed.
Subjects were categorized into 5 groups according to cardiovascular disease risk.

Group 1: Very high-risk group: The presence of established CVD plus
   (1)   Multiple major risk factors (especially diabetes)
   (2)   Severe and poorly controlled risk factors (especially continued cigarette smoking)
   (3)   Multiple risk factors of the metabolic syndrome(especially high triglyceride $\geq$ 200 mg/dL plus non-HDL-C$\geq$130mg/dL with TG$\geq$200mg/dL and HDL-C < 40)
   (4)   Patients with acute coronary syndromes

Group 2: High-risk group: coronary heart disease (CHD) or CHD risk equivalents† (10 year risk > 20%)

Group 3: Moderately high-risk group: 2+ risk factors ‡(10-year risk 10% ~ 20%)

Group 4: Moderate-risk group: 2+ risk factors‡(10-year risk <10%)

Group 5: Low-risk group: 0-1 risk factor

* Coronary heart disease includes myocardial infarction, atypical angina, coronary artery interventions (angioplasty or coronary artery bypass grafting), or clinically definitive myocardial ischemia

† CHD risk equivalents include any clinical forms of atherosclerotic diseases (peripheral artery disease, abdominal aortic aneurysm, carotid artery disease (transient ischemic attack or stroke originated from the carotid artery, diabetes, or 2+ CHD risk factors with a 10-year risk for CHD >20%.

‡ Risk factors include cigarette smoking, high blood pressure (BP >140/90mmHg or on antihypertensive drugs), low HDL-C <40 mg/dL, a family history of premature CHD (CHD in male first degree relative <55 years, CHD in female first degree relative <65 years), and age (men >45, women >55)

The criteria of this study were as bellows.

Inclusion criteria

Target patients are those who have records of clinic visit with circulatory and endocrine internal medicines of nationwide tertiary hospitals within the last one-year.
For inclusion in the study subjects must fulfill all of the following criteria:
1. Female and male aged 18 years or older.
2. Subjects with at least one clinic visit record within the last 12 months from the date of data entry.
3. Subjects with at least one hs-CRP level measured within the last 12 months from the date of data entry.

Exclusion criteria

Any of the following is regarded as a criterion for exclusion from the study:
1. Use of statins or other lipid-lowering therapies including fibrates, niacin, and bile acid sequestrants in the past 3 months prior to hs-CRP measurement
2. Active inflammatory diseases documented during the period of CRP measurement
3. Female subjects currently receiving oral hormone replacement therapy after menopause
4. Subjects taking immunosuppressants
5. Development of cancer documented in the last 5 years (except for non-malignant skin cancer)
6. Findings of chronic inflammation: arthritis, lupus, or inflammatory bowel disease.

The design of this study was descriptive and it had no predefined hypothesis. We summarized the data using descriptive statistics and analysis the data with exploratory method about any doubtable factors for primary objective.
For comparing among groups, we did use 5% significance level. And we made tables and figures for descriptive analysis such as demographic characteristics, presence of CHD risk factors, Lipid profile and C-reactive protein.

1st Evaluation

The portion of subject within normal range and statistical data of hs-CRP levels according to risk categories by the NCEP ATP III was estimated.

2nd Evaluation

The portion of subjects within normal range and statistical data of hs-CRP levels according to risk factor was estimated and a correlation coefficient between lipid profile including LDL cholesterol and concentration of hs-CRP was presented.

Further Evaluation

The risk factor and information of concomitant medication including statin was summarized and the portion of subjects within normal range and statistical data of hs-CRP levels was estimated according to statin treatment.

RESULTS:

The risk factor distribution

CHD risk factor has risk factors as aging, HTN, low LDL-C, smoking, High HDL-C, family medical history of acute coronary syndromes, sequentially. Risk factor of CHD or correspondence with CHD has CAD, DM, risk factor which is more than 20% risk of 10 years hard CHD, carotid artery disease, peripheral artery disease, abdominal aorta, sequentially. Metabolic syndrome factor has HTN, low HDL-C, high triglyceride, abdominal obesity, sequentially.

The Efficacy Evaluation

Throughout correlation between hs-CRP concentration and LDL target goal, subjects in very high risk group, who were the lowest LDL goal target group, were shown higher hs-CRP level and high portion of subjects with normal range.

As a result, LDL target goal is getting higher, hs-CRP level is getting lower, HDL is correlated with hs-CRP concentration, especially, hs-CRP increased when there is CHD or risk factor correspondence with CHD.