AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Crestor
ACTIVE INGREDIENT: Rosuvastatin

Study No: NIS-CBR-CRE-2007/1
Education and Awareness Program Targeting the Assessment of Adherence of the Treatment of Dyslipidemia - PRECAVER

Developmental Phase: Phase IV Study
Study Completion Date: 17/Sep/2010
Date of Report: 18 August 2011

OBJECTIVES:

To evaluate the benefit (level of treatment compliance), by reduction of LDL-C in the group of patients who have received a program of guidance reinforcement, in addition to that usually given by the physician, addressed to patients eligible for treatment with rosuvastatin compared to a control group, that is, those who have received solely the usual medical information.

Secondary objectives:

- Stratification of cardiovascular risk through Framingham score
- Stratification of patient profile (personal features) in regard to their health
- Stratification of socio-economic and cultural level

METHODS:

Non-interventional, open, randomized, prospective study.
Intervention through the Program of Guidance and Awareness X Non-Intervention (control group).
Patients who have received rosuvastatin were randomized into two groups, one have received periodic information as part of a reinforcement program with guidance addressed in regard to the level of pharmacological treatment compliance, and the other one have received medical information and advice as routinely done by the physician together with the prescribed treatment (in this case, rosuvastatin), this group was called control group.
Dosages of LDL-C were transcribed from the patient medical records before starting treatment, pre-identified for inclusion in the study, and then after 6 months. Measure of lipid profile should have been performed after fasting from 12 to 14 hours in subjects

with usual diet, stable metabolic status and weight for at least two weeks before examination was performed, according to the IV Brazilian Dyslipidemia Guideline.
The absolute change in LDL-C was the most important marker as compliance indicator.
The accomplishment of treatment goals of lipid lowering was less important because patients have not been preselected based in risk group or stratification related to the goals. However an analysis based on cardiovascular risk stratification has been predicted.

Target subject population

Six hundred patients from the region of Campinas, State of São Paulo, Brazil.

Investigational product and dosage

Not applicable

Statistical methods

It has been estimated that patients who received the guidance supplementary program (Active Group), in addition to the one usually given by the physician, could have had treatment compliance 30% higher than those who haven't received it (Control Group).
Therefore, considering a significance level of 5% and a power of 80%, 600 patients – 300 in each study arm – were sufficient in order to show superiority of the LDL-C control in patients receiving the supplementary guidance program.
The first analysis has been performed based on the intention-to-treat principles, including all patients, even those who have discontinued treatment. That analysis has been used to classify patients as responders or non-responders, for patients who have had discontinued treatment, the initial score of LDL-C was considered. The Chi-square test has been applied in order to help finding out differences between the study groups in terms of treatment characteristics and efficacy (understood by whether normal levels of LDL-C could have been reached or not).
All the spontaneously reported adverse events have been listed in regard to their frequency, intensity and causal relation.
The second analysis was restricted to patients who have had completed treatment or those who had discontinued treatment due to lack of efficacy, concurrent disease or due to the onset of adverse events.
The results have been analyzed through Statistic version 5.0 (Stat Soft, Inc - Tulsa - USA) software with the adoption of a significance level of 0.05 ($\alpha = 5\%$), and with the adequate adjustment performed when necessary.
Initially, the biodemographic and clinical data have been examined and checked in order to confirm if all patients were really eligible for the study.
Evaluations have included a description of the study population.
Qualitative (nominal) variables have been expressed as absolute (n) and relative (%) frequency. Quantitative (ordinal) variables have been expressed as mean, standard deviation, median, minimum and maximum values.
Laboratory tests have been analyzed through Analysis of Variance (ANOVA) for repeated measures in one factor, following confirmation of data normality (Kolmogorov-Smirnov test with Lilliefors correction) and homogeneity (Levene test).
The nonparametric Wilcoxon and Mann-Withney tests have been used after significance level (α) adjustment, if conditions to use ANOVA were not met, even following the data transformation technique.
Another objective for this project was to check whether the treatment compliance could have any relationship with the cardiovascular risk rating or the social, cultural and

economic levels of subjects. The Chi-square or The Fisher tests were used to verify whether those associations existed.
Although performance of the above mentioned tests have been predicted, their used depended on the encountered distribution, and the scheduled planning could have been subject to changes and, thus, parametric or nonparametric tests have been used.

RESULTS:

This non-interventional, open, randomized, prospective study, with 600 patients aimed to observe subjects in the region of Campinas regarding the adherence to treatment with rosuvastatin by reducing LDL-C values in the group that have received a program enhancement (Active) in relation to the one that have not received (Control) orientations of the Programme Guidance and Awareness. Both groups received usual medical advice.
It has been estimated that patients recipients of supplementary guidance (Active) could present a 30% adherence to treatment than those have not received sequential information (Control).
The Principles of Intention to Treat (ITT) analysis have been used. Including all patients, not excluding those who discontinued treatment or for any other reason regardless final scores. They have replicated the baseline score.

The study have included 592 subjects (299 in the Active Group and 293 in the Control Group) of which 63 in the active group and 62 of the control group have discontinued treatment or have a change in the conduct of observation. 82,3% and 82,6% of patients in the Active and Control groups have attended initial and final visits, with no difference between them.
The sample was homogeneous regarding demographic information and patients' medical history.
In the Control group, the mean age was 55,9 years, where 63,1% were female, 94,2% white, 43,7% reporting a household income of 5 to 10 minimum wages and 31,1% having completed the second degree of school, according to local standards / official educational levels.
In the Active group, the average age was 55,9 years with 62,2% of female patients, 95% white, 42,1% with a household income of 5 to 10 minimum wages and 34,1% having completed the second degree of school, according to local standards / official educational levels.
51,8% and 49,8% of patients have reported familial hypercholesterolemia and 68,6% and 63,5% have also reported other relevant medical history both in Active and Control groups, respectively.
Cardiovascular risk have been classified as low in 55,9% and 53,6% of patients and 78,9% and 78,8% primary prevention was indicated to subjective from Active and Control groups, respectively.
Initially, both groups showed no significant differences in results of LDL-C measures ($p=0.8115$), HDL-C ($p=0.8088$) and Total Cholesterol ($p=0.8074$), the Framingham Score ($p=0.1449$), Systolic ($p=0.4020$) and Diastolic ($p=0.1230$) Blood Pressure, heart rate ($p=0.8991$), weight ($p=0.2603$) and waist circumference ($p=0.0908$).
Conclusion: The authors concluded that after treatment with rosuvastatin with or without additional guidance, both groups have continued to have similar behaviors regarding adherence, with no statistical difference between them ($p=0.8196$), but LDL-C was effective in both groups, due to treatment efficacy with rosuvastatin.