AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Crestor® (Rosuvastatin)
ACTIVE INGREDIENT: rosuvastatin calcium

Study No: D3560L00072
ADAPT Study: A Diabetes Study to Treat A Population previously Not at Target. A 12-week, open-label, multi-center, prospective study evaluating the effect of individualizing starting doses of rosuvastatin according to baseline LDL-cholesterol levels on achieving cholesterol targets in type 2 diabetic patients previously treated with another statin and not at LDL-cholesterol targets.

Developmental Phase: IV
Study Completion Date: 28-Sep-2009
Date of Report: 20-Jul-2010

OBJECTIVES:

Primary objectives:

The primary objective of the study is to assess whether using rosuvastatin at starting doses appropriate for the degree of LDL-C reduction required would achieve LDL-C target of ≤ 2.0 mmol/L quickly with either no titration or just one titration step after 6 weeks of therapy in type 2 diabetic patients previously treated with another statin and not at LDL-C targets.

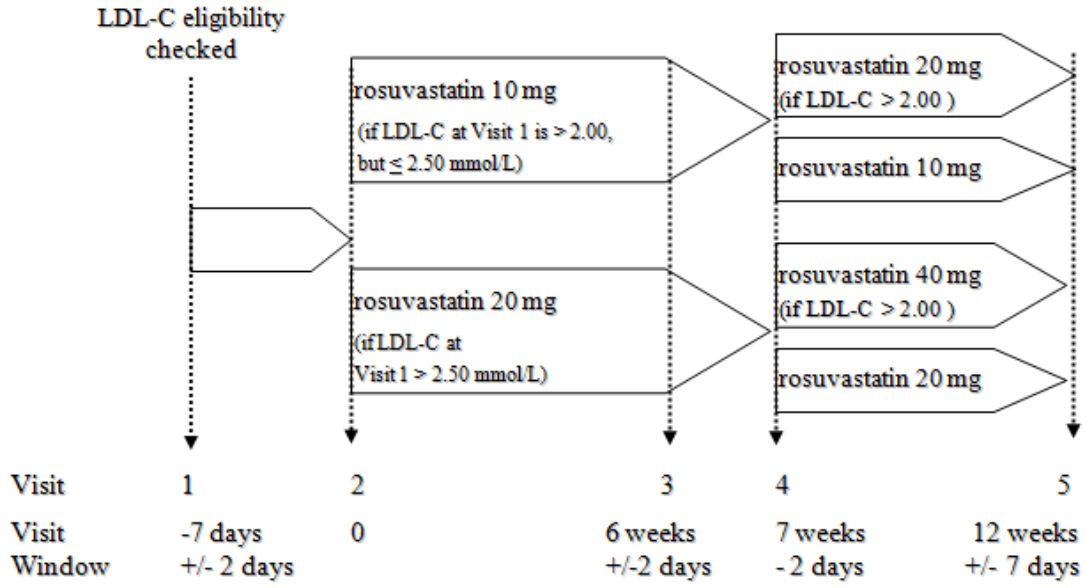
Secondary objectives:

1. To assess the proportion of subjects achieving TC/HDL-C ratio (i.e. TC/HDL < 4.0 mmol/L) at 6 and 12 weeks of treatment.
2. To assess the mean percent change in TC, LDL-C, HDL-C,TC/HDL-C ratio, Non-HDL-C, Triglycerides and ApoB/ApoA-1 ratio at 6 and 12 weeks.
3. To assess hsCRP value at week 6 and 12.
4. To determine the incidence of adverse events and abnormal laboratory values after 12 weeks of therapy.

METHODS:

This is an, open-label, multi-centre, prospective study.
At Visit 2, subjects will receive of open-label treatment with rosuvastatin 10 mg or 20 mg once daily according to their baseline (Visit 1) LDL-C level.
If LDL-C value from Visit 1 is > 2.00, but ≤ 2.50 mmol/L: patients will be receiving Rosuvastatin 10 mg.
If LDL-C value from Visit 1 is > 2.50 mmol/L: patients will be receiving Rosuvastatin 20 mg.
Subsequently;
Subjects who had not reached target LDL-C levels at 6 six weeks of treatment (Visit 3), will be titrated to the next highest dose of rosuvastatin (either 20 mg or 40 mg once daily) at their next visit (Visit 4) for an additional 5 weeks of therapy.
Subjects who had reached their target LDL-C levels at 6 weeks of treatment (Visit 3), at Visit 4 will continue with the initial rosuvastatin dose for an additional 5 weeks of therapy.

Figure 1 shows the design of the study and the sequence of treatment periods.
Figure 1 Flow chart of study design



RESULTS:

A total of 1044 patients were enrolled at 122 family practice sites, across Canada. Out of these, only 598 patients were allocated to treatment. The remaining 446 did not receive treatment as they did not fulfill the inclusion/exclusion criteria. The main reason for screen failures was LDL-C too low (55%), fasting glucose too high (11%) and triglycerides too high (8%).
The 598 patients who were allocated to treatment were grouped into two treatment arms: one arm where 319 patients received 10 mg of rosuvastatin as initial dose, while in the

other arm the remaining 279 patients received 20 mg of the drug as initial dose. At the 6-week assessment visit, out of the 319 patients in the first arm receiving 10 mg rosuvastatin as initial dose, 232 continued to remain on this dose, while 75 of them were titrated to the 20 mg dose and 12 patients discontinued the study. Similarly, out of the 279 patients receiving 20 mg of rosuvastatin as the initial dose in the second arm, 182 remained on 20 mg dose, while 79 were titrated to 40 mg and 18 patients discontinued the study.
The rosuvastatin treatment in this study was well tolerated. Adverse events were similar between both treatment arms and across all doses, with no reported incidences of: rhabdomyolysis, ALT > 3X ULN, CK > 10X ULN and no withdrawals secondary to rosuvastatin treatment.

At 12 weeks of treatment with or without titration, 82% of the patients met the primary endpoint of achieving a LDL-C target of ≤2.0 mmol/L, with 84% of the patients in the 10 mg group and 79% of the patients in the 20 mg group. Overall the LDL-C was reduced to 1.7 mmol/L in both the 10 mg and 20 mg groups. Furthermore, over 90% of patients who achieved LDL-C targets also achieved ApoB target < 0.8 g/L at week 12.