AstraZeneca

ZD4522/CN/01

SUMMARY

ASTRAZENECA PHARMACEUTICALS

ACTIVE INGREDIENT: Rosuvastatin calcium

Trial title (number): A 12-Week Randomised Double-blind Multicentre Trial to Evaluate the Efficacy and Safety of Rosuvastatin 10 mg and Atorvastatin 10 mg in the Treatment of Subjects With Hypercholesterolemia

Developmental phase: III
Study Start Date: 15 March 2004
Database Lock: 24 May 2005
Approval Date: 29 Dec 2006

OBJECTIVES

To evaluate the efficacy and safety of rosuvastatin 10 mg and atorvastatin 10 mg in the treatment of subjects with hypercholesterolemia.

METHODS

Multi-centre, randomised, double-blind, 2-arm, parallel-group, comparator trial

RESULTS

Demographic characteristics：
722 subjects entered dietary run-in period in this study. 304 subjects fulfilled the randomization criterias. Among these subjects, 201 subjects (66.1%) were randomized into rosuvastatin 10mg treatment group, 103 subjects (33.9%) were randomized into atorvastatin 10mg treatment group, the randomization ratio was 2:1. 14 (4.6%) subjects were discontinued from the randomization treatment period. 290 subjects were included in the ITT population. 263 subjects were included in the PP population. 301 subjects were included in the safety population.

Demographic characteristics were balance in 2 treatment groups. All the subjects were Chinese. 72.8% were females, 27.2% were males. 22.8% had CHD or CHD risk equivalents. 33.4% had multiple (2+) risk factors. 43.8% had 0-1 risk factor.

Efficacy outcome variables：
The baseline LDL-C level at the randomization point was 192.5 ± 20.2mg/dl.

The primary outcome variable, which is the percent change from baseline in LDL-C at 12 weeks, was 45.6% in rosuvastatin 10mg treatment group and 39.0% in atorvastatin treatment group in ITT population. The difference between these 2 groups was 6.6%, which was statistically significant (p=0.0003). This result was supported by the same analysis done in PP population (p=0.0001).

Among the secondary outcome variables, the percent changes from baseline in TC and ApoB at 12 weeks were greater in rosuvastain 10mg treatment group than the ones in atorvastatin 10mg

treatment group (TC 33.2%/28.6%，ApoB 40.3%/35.6%), the differences were statistically significant. The increase in HDL-C and ApoA-I, the reduction in TG were numeric greater in rosuvastatin 10mg treatment group than in atorvastatin 10mg treatment group (HDL-C 6.6%/4.3%，ApoA-I 12.5%/9.8%，TG 22.8%/16.6%). In addition, 78.0% subjects in the rosuvastatin 10mg treatment group reached the ATPIII LDL-C goal, while 72.7% in atorvastatin 10mg treatment group. This difference was more obvious in the population who had CHD or CHD risk equivalents, which was 56.5% and 35.0% respectively.

For the onset of efficacy, rosuvastatin 10mg showed the biggest lipid regulation effect after 6 weeks treatment, this effect was kept until 12 weeks at the end of this study.

Safety Evaluation Results:
The safety of both rosuvastatin 10 mg group and atorvastatin 10mg group is good. The adverse events (AEs) rate was 25.3% in rosuvastatin 10mg group, which is similar to 24.3% in atorvastatin 10mg group. Also there was no significant difference between these two groups by organ systemic categories. There were 3 patients in rosuvastatin 10mg group and 2 patients in atorvastatin 10mg group discontinued the study due to AEs. 1 patient in rosuvastatin 10mg group and 2 patients in atorvastatin groups had serious adverse events (SAEs). No dead case was reported through the whole study. No drug related SAEs happened based on investigator's judgement. There was no CK elevation greater than 10 times up-limit normal range or myopathy cases in the study. Only 1 case in rosuvastatin group, whose ALT elevation was a little bit greater than 3 times up-limit normal range, had no uncomfortable symptoms, and the ALT level came back to normal during the follow-up after the study. There were no other clinical significant changes in vital signs, laboratory variables, or ECG examinations.

Totally 29 patients entered the extension therapy period, 22 patients completed rosuvastatin 20mg treatment for 8 weeks. 4 patients reported mild and non-drug related AEs. 2 out of these 4 patients had the AEs ever since the randomisation period. No SAEs were reported. No myopathy happened, and no clinically significant liver enzymes elevation or other laboratory variables changed in this subgroup patients.

REFERENCE

Rosuvastatin Registration Clinical Trial Group. The efficacy and safety of rosuvastatin on treating patients with hypercholesterolemia in Chinese: a randomized, double-blind,multi-center clinical trial. Chin J Cardiol 2007;35(3): 207-211.

As with any comprehensive clinical trial programme, individual studies may include both approved and non-approved treatment regimens, including doses higher than those approved for clinical use. Before prescribing Crestor™ (rosuvastatin), Healthcare Professionals should view their specific country information.