

April 20, 2007

PRIME Program

**(Post-marketing Surveillance Study for Rosuvastatin: Innovative Medical Experience)
Report of Results of CRESTOR[®] Clinical Experience Investigation (CEI)
study of Approximately 10,000 Japanese Patients
- First Study in Japan to Conform to Pharmacovigilance Planning Guidelines -**

AstraZeneca K.K. (Head Office: Kita-ku, Osaka; President: Masuhiro Kato) and Shionogi & Co., Ltd. (Head Office: Chuo-ku, Osaka; President: Motozo Shiono) conducted a study to collect and evaluate safety information to confirm the safety profile for CRESTOR[®] for use by Japanese patients. This study was the first in Japan to conform to ICH-E2E¹ guidelines for pharmacovigilance planning. With the completion of the CEI for CRESTOR[®], we confirmed the drug's safety in Japanese patients, as follows:

- The final analysis of a Clinical Experience Investigation (CEI) study of 8,795 patients, as a part of the PRIME Program, showed an adverse drug reaction incidence of 11.12%, which did not exceed that reported as 18.8% in clinical trials at the time of approval.
- Regarding the CRESTOR[®] effect on muscle, liver and kidney, as specified in the pharmacovigilance plan to be actively monitored in this study, no new finding was found that suggests any difference between Japanese CEI data and overseas clinical data. Lab test analysis was employed for safety signal detection of effect on muscle, liver and kidney.
- Causal relationship with CRESTOR was not established for any unexpected ADR. As a conclusion, no new safety concern was found in this CEI study.

Summary of CEI Study [the PRIME Program]

Registration period: May 2005 – March 2006

Targeted patients : Patients with hypercholesterolemia or familial hypercholesterolemia who had not taken CRESTOR[®] .

Observation period: 12 weeks with the starting dose (including wash-out period), in case of dose increased during the first 12 weeks, followed by 12 additional weeks with the increased dose from commencement of the dose. In cases of dosage increase, the maximum observation period was 48 weeks from the start date of initial dose.

Registered patients: 9,668 initially and 9,661 at survey end

Safety evaluable patients: 8,795; Efficacy evaluable patients: 8,390

Safety

Adverse drug reaction cumulative incidence rate: 11.12% (978 of 8,795 safety evaluable patients)
 Main Adverse drug reaction: Blood creatine phosphokinase increased (201 events, 2.29%), Myalgia (126 events, 1.43%), Hepatic function abnormal (92 events, 1.05%), Blood urine present (62 events, 0.70%), Alanine aminotransferase increased (61 events, 0.69%), Gamma-glutamyltransferase increased (52 events, 0.59%), Aspartate aminotransferase increased (47 events, 0.53%)

Serious adverse drug reaction cumulative incidence rate: 0.34 % (37 events in 30 patients)
 Serious adverse drug reactions: Blood creatine phosphokinase increased (6 events); Hepatic function abnormal, Liver disorder (4 events each); Gastric ulcer haemorrhage², Pancreatitis and Drug eruption (2 event each); Angina pectoris², Sick sinus syndrome², Pancreatitis acute, Oedema², Bile duct stone², Cholecystitis acute², Cholelithiasis², Back pain², Musculoskeletal pain², Myalgia, Dizziness, Monoparesis², Tension headache, Nephrotic syndrome², Renal failure acute², Renal impairment² and Skin exfoliation² (1 event each)

Efficacy

- Administration of the starting dose of 2.5mg of CRESTOR[®] showed superior efficacy. LDL-Cholesterol (LDL-C) levels dropped by approximately 40% and HDL-Cholesterol (HDL-C) levels rose by 5.6%³.
- With CRESTOR 2.5mg, 86% of participants achieved the LDL-C control targets of the Guidelines for Diagnosis and Treatment of Atherosclerotic Cardiovascular Diseases (by the Japan Atherosclerosis Society)³.
- Excellent reduction of LDL-C levels was shown regardless of existing of past or concurrent diseases such as diabetes mellitus and metabolic syndrome.
- Increasing the dosage to 5mg was effective in further lowering LDL-C levels and raising HDL-C levels.

Notes:

1. ICH-E2E: Guidelines for post-marketing pharmacovigilance. These guidelines make provisions for identifying and preventing risks with the aim of supporting pharmacovigilance planning, especially in preparation for new drugs in the early post-marketing period.
2. Adverse drug reactions unexpected from the Precautions.
3. Patients who had not received any treatment drug for hypercholesterolemia for the three months preceding the start of CRESTOR[®].

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