AstraZeneca

4522AS/0004
STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Crestor™
ACTIVE INGREDIENT: rosuvastatin

Study No: 4522AS/0004
A randomised, double-blind, placebo controlled, crossover dose-ranging study to investigate the effect of rosuvastatin (CRESTOR®) on high density lipoprotein kinetics in patients with the metabolic syndrome.

Developmental phase: Phase IIb
Study start date: 15 April 2004
Study Database lock: 1 April 2006

OBJECTIVES:

Primary Objective
Determine the dose-related effect of treatment with rosuvastatin on production and fractional catabolism of apolipoprotein A-I (apoA-I) and apolipoprotein A-II (apoA-II), and on the plasma apoA-I, apoA-II and high-density lipoprotein cholesterol (HDL-C) concentration

Secondary Objectives
Determine the effect of treatment with rosuvastatin on:

- cellular cholesterol efflux.
- total cholesterol, low-density lipoprotein cholesterol (LDL-C), non-LDL-C, triglyceride and preβ1-HDL concentrations.
- HDL_2 :HDL_3 cholesterol ratio
- Cholesteryl ester transfer protein (CETP) and lecithin:cholesterol acyl transferase (LCAT) activity
- Lathosterol and campesterol, total apolipoprotein B (apoB), nonesterified fatty acids (NEFA) and apolipoprotein C-III (apoC-III) plasma concentrations.

METHODS

The purpose of this study was to investigate the dose-related effect of treatment with rosuvastatin on production and fractional catabolism of apolipoprotein A-I (apoA-I) and apolipoprotein A-II (apoA-II), and on the plasma apoA-I, apoA-II and high-density lipoprotein cholesterol (HDL-C) concentration. 25 patients entered the study of which 14 were randomised and 12 completed.

Inclusion Criteria
Signed informed consent, male aged 30 to 70 years of age, LDL-C <6 mmol/L, HDL-C ≤1.2 mmol/L, and at least 2 of the following:

- insulin resistance (fasting glucose >6 mmol/L or insulin >10 mU/L or HOMA score >2.5)
- central obesity (waist circumference ≥94 cm).
- plasma triglycerides ≥1.7 and <4.5 mmol/L.
- blood pressure ≥130/ ≥85 mm Hg or on drug treatment for hypertension

Exclusion Criteria

Key exclusion criteria include LDL cholesterol ≥6 mmol/L, pre-existing or history of cardiovascular disease, diabetes, renal dysfunction, anaemia, history of significant dyspepsia or gastrointestinal disease, apolipoprotein genotype E2/E2, plus others..

RESULTS

Ooi EM, Barrett PH, Chan DC, Nestel PJ, Watts GF. Dose-dependent effect of rosuvastatin on apolipoprotein B-100 kinetics in the metabolic syndrome. Atherosclerosis [Epub ahead of print] 2007 Apr 11; DOI: 10.1016/j.atherosclerosis.2007.03.004. Available from URL:http://www.atherosclerosis-journal.com/article/PIIS0021915007001670/abstract

Ooi EM, Watts GF, Nestel PJ, Sviridov D, Hoang A, Barrett PH. Dose-dependent regulation of high-density lipoprotein metabolism with rosuvastatin in the metabolic syndrome. J Clin Endocrinol Metab [Epub ahead of print] 2007 Nov 20: Doi:10.1210/jc.2007-0854. Available from URL:http://jcem.endojournals.org/cgi/content/abstract/jc.2007-0854v1