Thesis Title Efficacy and Safety of Fluvastatin Alone and in Combination with Fenofibrate or Cholestyramine in CHD Patients with Hypercholesterolemia

Name Chantaratsamon Dansirikul

Degree Master of Science (Pharmacy)

Thesis Supervisory Committee

Chuthamanee Suthisisang, Ph.D.

Banhan Koanantakul, M.D.

Jongjit Angkatavanich, M.Sc.

Phannee Pidatcha, M.Sc.

Date of Graduation 18 July B.E. 2540 (1997)

ABSTRACT

The efficacy and safety of fluvastatin were assessed in CHD patients with hypercholesterolemia who came to follow-up at the heart clinic of the Bhumipol Adulyadej Hospital during January 1996 until December 1996. The study consisted of two parts; 1) counseling about dietary consumption which should be maintained throughout the study and 2) drug therapy. Follow-up of the efficacy of intervention was performed by measuring blood lipid profiles (total cholesterol, HDL-C, TG, LDL-C, apo A-I and apo B) at the 4th week after dietary counseling and every 6 weeks after drug treatment. The goal of treatment was to lower LDL-C to the level of less than 100 mg/dL. If the LDL-C goal was not achieved after dietary counseling, drug therapy was added. Drug treatment was started with fluvastatin 20 mg/day for 6 weeks and then increased to 40 mg/day if LDL-C was not reduced to the desirable level. Finally the patients

were concomitantly received either micronized fenofibrate 200 mg/day or cholestyramine 4 g/day with fluvastatin 40 mg/day.

The study was performed in thirty-seven CHD patients which consisted of 22 males and 15 females. Mean age was 61.5 and 63.3 years, respectively. Mean LDL-C at the baseline was 182.3 mg/dL.

The results showed that dietary intervention for 4 weeks reduced LDL-C and apo B by 9.1% and 5.8%, respectively. However, HDL-C and apo A-I were also decreased by 5.4 and 3.4%, respectively, with the concurrent increasing in triglyceride level by 15.0%. None of the patients succeeded with LDL-C of less than 100 mg/dL. All of 37 patients received fluvastatin at the dose of 20 mg/day for 6 weeks. This regimen lowered LDL-C, apo B and triglyceride by 17.9, 19.5 and 6.4%, respectively, while HDL-C and apo A-I were elevated by 13.7 and 10.4%, respectively. There were 6 patients who had LDL-C less than 100 mg/dL. Thirty patients were titrated to 40 mg dose. The lipid lowering effect was the reduction of LDL-C by 22.9%, apo B by 28.4% and triglyceride by 12.9%. There were 5 patients who achieved the LDL-C goal.

The addition of micronized fenofibrate 200 mg/day to fluvastatin 40 mg/day on 11 patients showed further response in decreasing LDL-C and apo B level at the total change of 32.7% and 36.9%, respectively. This regimen also demonstrated the greatest effect in lowering triglyceride level (33.2%) and increasing in HDL-C (25.7%) and apo A-I (17.9%). The combination of fluvastatin 40 mg/day and cholestyramine 4 g/day on 12 patients demonstrated the highest effect in lowering LDL-C (40.1%) and apo B (42.7%) level.

At the end of the study, 34 patients completed the study. Eighteen patients (52.9%) succeeded with the goal of LDL-C < 100 mg/dL. Two patients

who received micronized fenofibrate 200 mg/day plus fluvastatin 40 mg/day and 5 patients who received the combination of cholestyramine 4 g/day and fluvastatin 40 mg/day had LDL-C less than 100 mg/dL.

Adverse drug events from fluvastatin included heart burn, GI disturbance, fatique, myalgia, pruritus and insomnia. One patient developed an increase in ASL and ALT greater than 3 times of the upper limits of normal value after treatment with fluvastatin 20 mg for 18 weeks. There were no clinically notable changes in CK and other routine laboratory data.

The result of this study revealed that fluvastatin is effective and well-tolerated in reducing blood cholesterol level either alone or in combination of fenofibrate or cholestyramine in CHD patients.