Rosuvastatin Is Efficacious as Monotherapy in Patients With Combined Dyslipidemia

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Cardiovascular disease (CVD) risk is greater in patients with combined dyslipidemia (CDL) than in those with isolated increases in fasting plasma triglyceride (TG) or low-density lipoprotein cholesterol (LDL-C) concentration. Effective treatment (Rx) of CDL has been confounded by: 1) concern of the increased risk of myopathy associated with combined use of a "statin" and a fibric acid; and 2) neglecting the effect of Rx on post-prandial (PP) lipemia. This study was initiated to test the hypothesis that the magnitude of reduction in both fasting and PP lipid metabolism in non-severely hypertriglyceridemic subjects with CDL would obviate the need for combined drug Rx. Forty nonobese subjects with CDL were randomly assigned to Rx with either RSV (10 mg/day) or gemfibrozil (GEM, 1200 mg/day) for 3 months, and multiple aspects of fasting and PP carbohydrate and lipid metabolism assessed before and after Rx. The two groups did not differ in age, sex distribution, or BMI. Mean±SE (mg/dL) fasting plasma LDL-C levels fell (p<0.001) following RSV-Rx (138±7 vs. 62±4), but did not change in GEM-treated subjects (126±5 vs. 128±4). Fasting TG levels fell (p<0.001), and to a similar degree in GEM-treated (284±17 vs. 166±23) and RSV-treated (324±19 vs. 211±18) subjects. RSV-treated subjects also had significantly greater decreases in apo B-100, apo E, and the apo B-100/apo A-1 ratio compared to those treated with GEM. Daylong glucose, insulin, and free fatty acid levels did not change with Rx, whereas PP-TG levels fell to a similar degree in both groups (P<0.01). Although the PP-remnant lipoprotein-C levels fell significantly with Rx in both groups, the magnitude of the change was greater in the RSV-Rx group (P<0.005). Finally, RSV-Rx resulted in significant (p<0.001) reductions in C-reactive protein (median change -9.1%). These results demonstrate that RSV provides effective mono-therapy to decrease lipoprotein-related CVD risk factors in subjects with CDL.

Analysis of the Renal Safety of Atorvastatin in a Broad Spectrum of Patients With Dyslipidemia

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Background: This report summarizes the renal safety data from >9000 patients exposed to atorvastatin for up to 2 years in completed clinical trials. These data are especially important in the current climate which has seen increased scrutiny placed on all aspects of the safety of chronic statin therapy.

Methods: Data were analyzed from 16,731 dyslipidemic patients (9076 male/6755 female; median age 61 yrs) enrolled in 44 clinical trials. The studies included 9416 atorvastatin-treated patients, 1789 placebo-treated patients and 5526 patients treated with other statins (simvastatin [2771]; pravastatin [807]; lovastatin [968]; fluvastatin [744]; cerivastatin [296]). A broad spectrum of dyslipidemic patients with varying risks for cardiovascular disease were evaluated for up to 2 years.

Results: Across the 44 studies analyzed, renal adverse events were rare in all 3 treatment groups. Albuminuria was observed in 7 patients receiving atorvastatin (0.07%), compared to 5 patients receiving other statins (0.09%) and 0 patients receiving placebo. No case of albuminuria was considered to be treatment related. The rate of occurrence of hematuria was also low in all treatment groups (atorvastatin, 4 patients [0.05%]; other statins, 34 patients [0.6%]; placebo, 3 patients [0.2%]). Only in 1 atorvastatin and 1 placebo patient was hematuria considered to be possibly associated with study treatment. In the subset of patients treated in placebo-controlled trials, there were no cases of albuminuria for either placebo or atorvastatin and hematuria was observed in 0.2% of patients treated with placebo (3/1789) and in 0.3% of patients treated with atorvastatin (8/2976). Data were analyzed from 16,731 dyslipidemic patients (9076 male/6755 female; median age 61 yrs) enrolled in 44 clinical trials. The studies included 9416 atorvastatin-treated patients, 1789 placebo-treated patients and 5526 patients treated with other statins (simvastatin [2771]; pravastatin [807]; lovastatin [968]; fluvastatin [744]; cerivastatin [296]). A broad spectrum of dyslipidemic patients with varying risks for cardiovascular disease were evaluated for up to 2 years.

Conclusion: Specific analysis of renal adverse events in 44 clinical trials demonstrates that these occurred infrequently with atorvastatin and at similar rates to placebo. These data provide further evidence to support the favorable clinical safety profile of atorvastatin 10 mg to 80 mg in a broad range of patients.

Changes in Renal Burden of Lipid-Metabolism by Lipid-Lowering Therapy With Atorvastatin: Serial Evaluation by Coronary Angiography

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Background: The concept of coronary plaque stabilization by statin therapy has been clarified. However, serial changes of coronary plaques by statin therapy in human have not been examined in detail.

Methods: Thirty-one patients with coronary artery disease were divided into either the comparison group (n=16) or the atorvastatin group (n=15). Before treatment and 12 months after, the color and complexity of 145 coronary plaques were determined according to angioscopic findings. The yellow score of the plaque was defined as 0 (white), 1 (light yellow), 2 (yellow), or 3 (dark yellow), and its disrupted score was defined as 0 or 1 score. Change in the mean yellow score and the change in LDL-C levels (r=0.81, p<0.0001). After dose titration, 18% of PR achieved LDL goal compared to 71% of GR (p<0.001). % LDL-C decrease after dose titration correlated with initial sex distribution, or BMI. Mean±SE (mg/dL) fasting plasma LDL-C levels fell (p<0.001) following RSV-Rx (138±7 vs. 62±4), but did not change in GEM-treated subjects (126±5 vs. 128±4). Fasting TG levels fell (p<0.001), and to a similar degree in GEM-treated (284±17 vs. 166±23) and RSV-treated (324±19 vs. 211±18) subjects. RSV-treated subjects also had significantly greater decreases in apo B-100, apo E, and the apo B-100/apo A-1 ratio compared to those treated with GEM. Daylong glucose, insulin, and free fatty acid levels did not change with Rx, whereas PP-TG levels fell to a similar degree in both groups (p<0.01). Although the PP-remnant lipoprotein-C levels fell significantly with Rx in both groups, the magnitude of the change was greater in the RSV-Rx group (p<0.005). Finally, RSV-Rx resulted in significant (p<0.001) reductions in C-reactive protein (median change -5.6%) compared to GEM-Rx (median change -9.1%). Conclusion: These results demonstrate that RSV provides effective mono-therapy to decrease lipoprotein-related CVD risk factors in subjects with CDL.

Efficacy of Ezetimibe-10 mg/Day Coadministered With Multiple Doses of Simvastatin in Patients With Primary Hypercholesterolemia

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Background: The cholesterol absorption inhibitor, ezetimibe (EZE), has a complementary mechanism of action to statins, which inhibit hepatic cholesterol synthesis. The purpose of this study was to evaluate the LDL-C-lowering efficacy of EZE 10 mg/day coadministered with simvastatin (SIM) 10, 20, 40, and 80 mg in hypercholesterolemic patients (pts).

Methods: This was a 12 wk multicenter, double-blind, randomized, placebo (PBO)-controlled, 4-arm trial. After a 4-wk PBO/diet run-in, 887 pts with LDL-C 145 - 250 mg/dL and TG ≤250 mg/dL, were randomized to one of ten daily treatments: PBO: EZE 10 mg; SIM: 10, 20, 40, or 80 mg; EZE 10 mg + SIM 10, 20, 40, or 80 mg.

Results: % LDL-C response for LDC-C, non-high density lipoprotein cholesterol (non-HDL-C), triglycerides (TG), and HDL-C by dose are summarized in the table. Plotted across the dose ranges, EZE-SIM was more effective (p<0.001) than SIM in reducing LDL-C (-53.1% ± -38.3%), TG (-28.0% ± -15.2%) and non-HDL-C (-48.5% ± -34.1%), while HDL-C was increased by 8% in both groups. A greater proportion of EZE-SIM pts reached the LDL-C target of <100 mg/dL (p<0.001; 82.4% (n=353) vs. 42.9% (n=345). Coadministration of EZE+SIM was well tolerated and had an overall safety profile similar to that of simvastatin monotherapy. However, there were more cases of prospective ≥2 x upper limit of normal elevations of aminotransferases in the EZE-SIM group vs. SIM group.

Conclusions: Overall, EZE-SIM was well tolerated and provided superior lipid-modifying efficacy over SIM monotherapy.

Efficacy of Ezetimibe Coadministered With Simvastatin Versus Atorvastatin in Patients With Hypercholesterolemia

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Background: This study was designed to evaluate the efficacy and safety of ezetimibe coadministered with simvastatin (EZ/S) vs atorvastatin (A) in adults with hypercholesterolemia.

Methods: After a 4-week diet/placebo run-in period, eligible patients were randomized 1:1:1 to 3 treatment groups, each for four 6-week periods: (1) A10 mg titrated to A20 mg, A40 mg, and A80 mg through Periods 1-4; (2) EZ/S 10 mg (10/10) titrated to EZ/S 20 mg.