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) concentrations. 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 achievement in both fasting and PP lipid metabolism in nondiabetic subjects with combined dyslipidemia may be improved by a "statin" that inhibits both cholesterol synthesis and PP lipemia. 

Methods: 1,084 patients with CDL were randomly assigned to Rx with either rosuvastatin (RSV; 10, 20, 40, or 80 mg) or gemfibrozil (GEM; 1200 mg/day) alone or coadministered with simvastatin (SIM) 10, 20, 40, or 80 mg.forty nondiabetic subjects with CDL were randomly assigned to Rx with either RSV (40 mg/day) or gemfibrozil (GEM, 1200 mg/day) for 3 months, and multiple aspects of fasting and PP lipid and lipoprotein metabolism was determined before and after Rx. The two groups did not differ in age, sex distribution, or BMI. Means±SE (mg/dL) fasting plasma LDL-C levels (P<0.001) followed RSV-Rx (138±7 vs. 62±4), but did not change in GEM-treated subjects (126±5 vs. 131±5). 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 changes 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 RSV in both groups, the magnitude of the change was greater in the RSV-Rx group (P<0.05). Finally, RSV-Rx resulted in significant (P<0.001) reductions in C-reactive protein (median change -57.6%) compared to GEM-Rx (median change -9.1%). Conclusion: In addition to the expected increases in LDL-C in the RSV group and PP Rx concentrations of TG-rich lipoproteins in RSV-treated subjects were equal to or greater than that seen with GEM-Rx. These results demonstrate that RSV provides effective mono-therapy to decrease lipoprotein-remnant 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/7575 female; median age 61 years) enrolled in 44 clinical trials. The studies included 9416 atorvastatin-treated patients, 1789 placebo-treated patients and 5526 patients treated with other statins (simvastatin [2717]; pravastatin [807]; lovastatin [968]; fluvastatin [744]; cerivastatin [260]). A broad spectrum of dyslipidemic patients with varying risks for cardiovascular events 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 (8/2987).

Conclusions: 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.

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 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 study. 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: Results for LDL-C, non-HDL-C, triglycerides (TG), and HDL-C by dose are summarized in the table. Pooled across the dose ranges, EZE-SIM was significantly more effective (P<0.001) than SIM in reducing LDL-C (-53.1% vs. -38.3%), TG (-28.0% vs. -15.2%) and non-HDL-C (-48.5% vs. -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 <100mg/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 SIM monotherapy. However, there were more cases of concomitant ≥2 x upper limit of normal elevations ofaminotransferases in the EZE-SIM group vs. SIM group.

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