Atorvastatin vs. Rosuvastatin in Protecting Kidneys

Results of two related trials investigating the effects of statins on urinary protein excretion and kidney function found atorvastatin (ATV) protective and rosuvastatin (RSV) unprotective, and possibly harmful, in diabetic and nondiabetic patients....

High-dose ATV significantly reduced proteinuria and did not affect renal function, whereas RSV was associated with a significant decline in function and had no effect on proteinuria, according to results of the PLANET trials, reported by Dick de Zeeuw, MD, PhD, a clinical pharmacologist and clinical trialist at the University Medical Center in Groningen, the Netherlands.

In diabetic and nondiabetic patients, proteinuria is a risk factor for further loss of kidney function and progression to end-stage renal disease, even when angiotensin-converting-enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) are used to lower blood pressure. Experimental results have suggested that statins reduce proteinuria and preserve kidney function, but clinical studies have produced mixed results.

The ongoing Study of Heart and Renal Protection (SHARP) trial with simvastatin and ezetimibe aims to test this hypothesis. Data collection is scheduled to complete in late summer 2010.

The two randomized double-blind multinational PLANET trials tested the effects of ATV 80 mg/day or RSV 10 or 40 mg/day on urinary protein excretion and renal function in hypercholesterolemic patients with moderate proteinuria.

PLANET I involved 325 patients with Type 1 or 2 diabetes, and PLANET II involved 220 patients without diabetes in the intent-to-treat populations. Patients had urinary protein/creatinine ratios of 500 to 5000 mg/g, a fasting low-density-lipoprotein (LDL)-cholesterol level of 90 mg/dL or higher, and had used ACE inhibitors or ARBs for at least 3 months prior to screening.

Patients with severe renal disease, defined as an estimated glomerular filtration rate (eGFR) below 40 mL/min per 1.73 m^2, or PLANET I patients with a hemoglobin A_{1c} level above 11% were excluded from the study, as were people with active liver disease.

The primary end point of the studies was the change in urinary protein/creatinine ratio from baseline to week 52 or to the last on-treatment observation carried forward. In PLANET I, the 3 treatment groups were fairly well matched at baseline for age (range, 57 to 59 years), sex (62% to 77% male), mean body mass index (BMI) (31.8 to 32.5 kg/m^2), mean blood pressures (138 to 139/79 to 80 mm Hg), mean eGFR (68.8 to 72.6 mL/min per 1.73 m^2), geometric mean protein/creatinine ratio (1160 to 1260 mg/g), and geometric mean albumin/creatinine ratio (805 to 911 mg/g).

Dr. de Zeeuw summarized the findings of both studies. For PLANET I (diabetic patients), he said, "atorvastatin significantly reduces the proteinuria in these patients on top of ACE/ARB therapy, with around a 15% reduction in proteinuria, whereas rosuvastatin, both 10 and 40 mg, had no significant effect at all on proteinuria."

The effect of ATV was evident by week 26 and continued through week 52, but neither RSV dose lowered proteinuria at either time point.

In PLANET II (the nondiabetic cohort), "we see a similar pattern, even more pronounced," he said. ATV reduced proteinuria by more than 20% at 26 and 52 weeks, but there was no significant effect with either dose of RSV. The results for albuminuria were very similar to those for proteinuria.

For eGFR, Dr. de Zeeuw said the results were "very surprising," in that in the PLANET I trial, patients on RSV lost more kidney function over 52 weeks than did those on ATV. Patients on ATV lost about 1 to 2 mL/min per 1.73 m^2 over 52 weeks, those on RSV 10 mg/day lost about 4 mL/min per 1.73 m^2, and those on RSV 40 mg/day lost close to 8 mL/min per 1.73 m^2.

In nondiabetic patients (PLANET II), the effects of the treatments on kidney function were slightly less pronounced. There was a significant decline in eGFR with RSV 40 mg/day but not in the other 2