Statins Improve Renal Function in Heart Patients

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ATLANTA — Intensive atorvastatin therapy in patients with stable coronary heart disease resulted in impressive improvement in kidney function over the course of 5 years in a post hoc analysis of the landmark Treating to New Targets trial, Dr. James Shepherd reported at the annual meeting of the American College of Cardiology.

A dose of 10 mg/day of atorvastatin (Lipitor) in TNT also thwarted the anticipated age-related decline in renal function, but the benefit was significantly greater with 80 mg/day, according to Dr. Shepherd of the University of Glasgow.

"Given that renal disease is now recognized as an important and independent predictor of increased cardiovascular risk, any delay in progression of renal disease has to be a good thing," he observed. "Pushing the dose of atorvastatin—or of any statin, for that matter—should give you lower LDL and will more greatly improve renal function over the course of time, according to these results."

TNT was a double-blind study in which 10,001 patients with stable coronary disease were randomized to 10 or 80 mg/day of atorvastatin and followed for 5 years. The primary end point was major coronary events, which showed a 22% relative risk reduction with high-dose therapy.

The new post hoc renal analysis involved nearly 8,000 TNT participants with baseline and follow-up measurements of creatinine clearance. Glomerular filtration rate (GFR) was estimated using both the Cockcroft-Gault formula and the abbreviated Modification of Diet in Renal Disease (MDRD) equation, which is considered by most nephrologists to be more reliable.

The typical annual age-related decline in renal function is 1-2 mL/min per 1.73 m^2 in patients with good blood pressure. But this tail off wasn't seen in TNT. Instead, estimated GFR by MDRD actually increased from a mean baseline of 65 mL/min per 1.73 m^2 by 5.6% over the course of 5 years in patients assigned to 10 mg/day of atorvastatin, and by a significantly greater 8.4% in the 80-mg group.

Among the roughly one-third of TNT participants with baseline stage 3 or worse chronic kidney disease as defined by a GFR of less than 60 mL/min per 1.73 m^2, significantly more in the high-dose atorvastatin group improved to less than stage 3 disease.

Moreover, significantly fewer patients in the high- than the low-dose atorvastatin group declined from a baseline GFR of at least 60 mL/min per 1.73 m^2 to stage 3 or worse chronic kidney disease.

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DR. SHEPHERD

The clinical significance of what Dr. Shepherd termed "these exciting data" lies in the fact that an estimated 8 million Americans have stage 3 chronic kidney disease—defined by a GFR of 30-59 mL/min per 1.73 m^2—or worse, with stage 3 being the threshold at which significant increases in cardiovascular events and all-cause mortality are seen. If individuals with earlier stage disease are included, an estimated 20 million Americans have chronic kidney disease.

On-treatment LDL-cholesterol levels averaged roughly 100 mg/dL with 10 mg of atorvastatin and 80 mg/dL with 80 mg of the statin. On-treatment LDL-cholesterol levels correlated with GFR improvement such that the lower the LDL cholesterol, the greater the improvement over time in GFR.

High-dose atorvastatin was not associated with additional safety concerns in TNT. Thus, high-dose therapy conferred greater reduction in cardiovascular risk with the added benefit of improved renal function—and with no additional safety issues, compared with low-dose therapy, Dr. Shepherd said.

The mechanism of the renal benefit documented in TNT is unclear, but the fact that on-treatment LDL cholesterol was a predictor of GFR improvement suggests the benefit comes from lowered LDL cholesterol levels. A lower LDL cholesterol level likely translates into more improvement in endothelial function and renal blood flow, he said.

TNT was funded by Pfizer Inc. Dr. Shepherd is a member of the study's steering committee and a consultant to Pfizer. ■