

Drug provides health benefits to diabetics with kidney disease

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A drug called atrasentan provides health benefits for patients who have both diabetes and kidney disease, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN). The findings suggest that atrasentan may help maintain the well-being of many patients who are at high risk of experiencing serious medical problems.

Individuals with type 2 diabetes have a [high risk](#) of developing additional health problems such as kidney and cardiovascular diseases. To reduce these risks, it is important to [lower blood pressure](#) and urinary protein excretion, or [albuminuria](#). Agents called renin-angiotensin-system (RAS) inhibitors can reduce both of these; however, [patients'](#) risk of experiencing residual albuminuria remains high.

Atrasentan, which targets the endothelin receptor A and was initially developed to treat cancer, is known to reduce albuminuria. In two identically designed, parallel, multinational, double-blind studies, researchers tested the potential for atrasentan to further reduce albuminuria in patients who had both type 2 diabetes and [kidney disease](#) and were taking RAS inhibitors. A total of 211 patients were randomized to placebo, 0.75 mg/day atrasentan, or 1.25 mg/day atrasentan for 12 weeks. Patients in the study had CKD stages 2 and 3 with albuminuria and were also receiving maximum tolerated doses of RAS inhibitors. "This represents a patient population with the highest unmet medical need among those with diabetes," said Dick de Zeeuw, MD (University Medical Center Groningen, in the Netherlands).

Dr. de Zeeuw and his colleagues found that the low dose of atrasentan, lowered albuminuria by 36% without major side effects. In addition, atrasentan lowered blood pressure and cholesterol levels. The higher dose lowered albuminuria to a similar extent but caused more fluid retention. "Although atrasentan increased weight, the incidence of peripheral edema, congestive heart failure, and other adverse events was similar between treatment groups," said Dr. de Zeeuw. While the precise mechanism by which atrasentan protects the kidneys is unclear, it's thought that the drug has beneficial effects on blood vessels in the kidneys while also reducing kidney inflammation and scarring.

"Although this study demonstrates that atrasentan treatment results in clinically significant albuminuria reduction with minimal fluid overload-related or cardiovascular side effects, a larger study on hard renal and/or cardiac outcomes is needed to further support these findings," said Dr. de Zeeuw. A larger ongoing phase 3 study (SONAR; ClinicalTrials.gov identifier NCT01858532) will shed more light on the kidney and cardiovascular protective effects of atrasentan.

In an accompanying editorial, Kiran Chandrashekar, MD and Luis Juncos, MD (University of Mississippi) noted that there is a critical need to develop additional therapies to improve the treatment of diabetic nephropathy and that endothelin inhibitors hold considerable promise. "This study was a success in that they identified a dose of atrasentan that provided a favorable risk/benefit ratio in the patient population studied, therefore providing a dose that will be used in future studies," they wrote. "While this is a positive step forward, it should be noted that this is just one of several steps that need to be taken."

More information: The article, entitled "The Endothelin Antagonist Atrasentan Lowers Residual Albuminuria in Patients with Type 2 Diabetic Nephropathy," will appear online at jasn.asnjournals.org/ on April 10, 2014.

The editorial, entitled "Endothelin Antagonists in Diabetic Nephropathy: Back to Basics," will appear online at jasn.asnjournals.org/ on April 10, 2014.

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