

Experimental drug more effective in treating rare kidney disease

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An experimental drug is more than twice as effective as the standard treatment at reducing a key measure of severity in a rare kidney disease. This is the finding of a phase II clinical trial published online October 25th in the *Journal of the American Society of Nephrology*.

The new study found that patients with focal segmental glomerulosclerosis (FSGS) taking the drug sparsentan saw a 45 percent reduction in proteinuria—an excess of protein in the urine that suggests poor kidney health. This compared to a 19 percent reduction in the group receiving the typically prescribed irbesartan.

"This is the first large-scale clinical trial of a treatment designed specifically to target FSGS, a rare disorder estimated to affect up to 40,000 people in the United States, and for which there are currently no approved therapies," says principal investigator and lead study author Howard Trachtman, MD, professor in the Department of Pediatrics at NYU School of Medicine and director of the division of pediatric nephrology at Hassenfeld Children's Hospital at NYU Langone. Nearly half of affected patients will progress to [end-stage kidney disease](#), he says.

"Not only could sparsentan become part of the standard of care for patients with FSGS, but there are potential implications for any patient with kidney disease characterized by proteinuria—including the more common IgA nephropathy which affects hundreds of thousands of people worldwide," says Dr. Trachtman.

Nephrologists use proteinuria as a measure, or marker, of the health of FSGS patients. When healthy, the kidneys filter blood, divert waste into urine, and return useful proteins to the bloodstream. FSGS, along with more common kidney diseases, damage the kidney's filtering units, with proteins passing through, and entering the urine to cause scarring in kidney tubules.

With no approved treatments for FSGS, the field has sought to apply to it medications developed to treat other diseases, says Trachtman, including angiotensin II receptor blockers (ARBs) like irbesartan. Initially developed to treat high blood pressure, ARBs are currently used in lieu of an approved FSGS therapy. These drugs act by lowering the blood pressure within the filtering units of the kidney and reducing kidney scarring.

New Approach

For the new study, researchers enrolled 109 patients with FSGS, ages 8-75 in the US and 18-75 in Europe, in a randomized, double-blind, active-controlled trial (DUET) across 44 sites to assess the efficacy and safety of sparsentan. Participants were assigned either escalating doses of sparsentan (200, 400, or 800 mg per day) or irbesartan in 300 mg per day doses over eight weeks. After completing the double-blind eight-week treatment period, patients were able to continue to receive sparsentan in an open-label treatment period.

The study medication, sparsentan, works both as an angiotensin II receptor blocker like irbesartan, and as a blocker of the action of a second protein, endothelin receptor type A (ETA). The study authors had hypothesized that the two actions would together limit the production of molecules that lead to kidney scarring more than irbesartan's single mechanism.

Sparsentan was indeed found to be more effective, and also to have very few serious side effects, with the most common—low [blood pressure](#), dizziness, and swelling—similar in both groups. The research team also found that combining effects in a single molecule increased patients' likelihood of taking their treatment because it reduced the number of pills.

Further study is needed to determine the long-term

effects of sparsentan on preservation of kidney function, say the authors. In addition to the open-label treatment period of DUET, a phase III clinical trial (DUPLEX) is actively enrolling patients to determine if sparsentan brings about a sustained reduction of proteinuria.

"The prevalence of FSGS is on the rise, and this combined therapy could offer new hope for [patients](#) with this rare [kidney](#) disorder who currently face a progressive decline, a high chance of end-stage [kidney disease](#), dialysis or transplantation," says Dr. Trachtman.

More information: Howard Trachtman et al, DUET: A Phase 2 Study Evaluating the Efficacy and Safety of Sparsentan in Patients with FSGS, *Journal of the American Society of Nephrology* (2018). [DOI: 10.1681/ASN.2018010091](https://doi.org/10.1681/ASN.2018010091)

Provided by NYU Langone Health

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