

Fibrosis and FSGS, a review of the FONT study

FSGS occurs in the functional units of the kidneys within the glomeruli, tiny blood vessels that function in the filtration of blood¹. The glomeruli normally allow small particles to pass through and form urine while preventing larger molecules such as proteins from leaving the blood. FSGS attacks the glomeruli resulting in a break down in this filtering mechanism and the leakage of proteins from the blood into the urine (proteinuria)¹.

As FSGS progresses, podocytes (special cells of the filtering unit) are lost and scarring or fibrosis develops². Fibrosis is the irreversible scarring of tissue which reduces the ability of organs such as the kidney to function properly. If the progression of the disease cannot be stopped with traditional medications, it can result in end-stage renal disease (ESRD) requiring dialysis or a kidney transplant for survival¹. This is the case in many patients with steroid resistant FSGS.

While treatment options are limited for patients affected by FSGS, hope may be on the horizon with a category of drugs called antifibrotics. These medications attempt to decrease or prevent the development of fibrosis, which would help to preserve kidney function, decrease the level of proteinuria and delay or prevent progression to ESRD.

Recently, in the *Clinical Journal of the American Society of Nephrology*, the results of a phase I clinical trial was published evaluating the safety and tolerability of rosiglitazone in patients diagnosed with steroid resistant FSGS. Rosiglitazone, an antidiabetic medication, has been shown to improve kidney function in animal models of FSGS and was evaluated as an antifibrotic medication. The primary goal of the study was to assess the safety and tolerability of rosiglitazone in patients that are diagnosed with steroid resistant FSGS³.

Eleven patients who had previously tried and failed traditional medications such as corticosteroids, calcineurin inhibitors as well as other immunosuppressive agents were included in the study. The patients received rosiglitazone for a dose of 3mg/m² per day for 16 weeks. There were no reports of serious side effects and medication was well tolerated by all patients³.



The researchers also evaluated how rosiglitazone was metabolized in the body, for instance, how much of the drug stays in the body and for how long. In addition to this, they evaluated how other factors such as kidney filtration rate and the amount of the protein albumin in the blood as well as the patient's demographic factors affected the activity of the drug³. This is necessary when defining the appropriate dosing for patients.

Based on these results, it was determined that the drug may have the potential to protect kidney function in these patients and that there is rationale to evaluate rosiglitazone as an anti-fibrotic medication for resistant FSGS in Phase II and III clinical trials. A phase I clinical trial determines whether the drug in question is safe for patients and what the appropriate dose of the drug should be but does not focus on the effectiveness of the drug. Phase II and III clinical trials are necessary to evaluate the drug's effectiveness.

1. Fehally J, Floege J, Johnson R. Comprehensive Clinical Nephrology.3. Philadelphia: Mosby Elsevier, 2007. Print.
2. Kaplan B, Meyers, K. Pediatric nephrology and urology: The requisites in pediatrics.3.Philadelphia: Mosby Elsevier, 2004. Print
3. Joy M, Gipson D, Dike M, Powell L, Thompson A, Vento S, Eddy A, Fogo A, Kopp J, Cattran D, Trachtman H. Phase I trial of Rosiglitazone in FSGS: I. Report of the FONT study group. Clin J Am Soc Nephrol 2009, January; 4(1):39-47.

