Study of the Clinical Efficacy and Safety of Finerenone for the Treatment of IGA Nephropathy

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Background

Primary IgA nephropathy (IgAN) is an immunopathological diagnostic term for a type of glomerulonephritis characterized by the deposition of IgA or IgA-dominant immune complexes in the glomerular tunica albuginea. And in China IgA nephropathy accounts for about 45% of primary glomerular diseases and about 26% of renal biopsies in patients with chronic failure. Among them, about 15-40% of IgA nephropathy patients progress to renal failure after 10-20 years; IgA nephropathy has become one of the main causes of end-stage renal failure. Therefore, active and effective treatment of IgA nephropathy and delaying the progression of the disease will play a positive role in improving the prognosis of patients, enhancing their quality of life, saving medical resources and reducing the burden of the society and families. For patients with end-stage renal disease, renal replacement therapy has a limited role. Since the pathogenesis of IgA nephropathy is still unclear, there is no sure and effective treatment option until now. Until now, the prognosis can be improved by early intervention to preserve renal function through non-pharmacological strategies and drugs targeting renal disease. For example, ACEI/ARB, SGLT2 drugs, but according to the current pharmacological regimen, some patients will still progress to renal failure. Therefore, new tools are needed.

The non-steroidal glucocorticoid receptor antagonist (MRA)- finerenone reduces the risk of composite renal outcomes, ESKD or renal death in patients with type 2 diabetes and CKD. This was demonstrated in the FIDELIO-DKD and FIGARO-DKD trials. Therefore, in the 2022 KDIGO guidelines, NSAID MRAs are recommended for use in patients with type 2 diabetic nephropathy with normal serum potassium and albuminuria >30 mg/g. According to the current guideline recommendations, NSAID MRAs have limited indications. Therefore it is necessary to conduct clinical studies to explore the scope of clinical indications for finerenone.

Study design and Methods:

This study was a retrospective, non-interventional, multi-centered, observational study. The study started collecting patients in December 2022 and completed in February 2024. Patients diagnosed with IgA nephropathy of any histology who were treated according to standardized practices according to the KDIGO glomerulonephritis guideline, and who were treated for the first time with finerenone were included. The inclusion criteria were age 18 to 75 years, primary IgAN diagnosed by renal biopsy, receive the highest tolerable dose of RASI inhibitors for at least 3 months, serum potassium <5 mmol/L and protein-to-creatinine ratio (PCR) >0.3 mg/g. The exclusion criteria included secondary IgAN, autosomal dominant polycystic kidney disease or autosomal recessive polycystic kidney disease, lupus nephritis, previous renal transplantation, malignant tumor, active malignancy, heart failure with ejection fraction <40% and followed up less than 6 months. Patients will also be excluded if they stop taking their medication on their own during the follow-up observation period.

This study was conducted at the Fourth Affiliated Hospital of Zhejiang University School of Medicine, the First Affiliated Hospital of Zhejiang University School of Medicine and Jinhua Municipal Centeral Hospital Medical Group. This study was approved by the Ethics Committees of the Fourth Affiliated Hospital of Zhejiang University School of Medicine.

The primary end point was percentage change in PCR from baseline to 6 months. The

secondary end point contained percentage change in PCR from baseline to 1, 2 and 3 months, frequency of patients with a 30% and 50% decrease in PCR and the level of change in clinical indicators, such as eGFR, serum creatinine, albumin, blood sodium and etc.. The focus of the safety analysis was on serious adverse events, decrease in eGFR of more than 30% and 40% from baseline, and hyperkalemia.

We collected clinical data at months 0, 1, 3, and 6 after the use of the drugs by following up and enquiring about their consultation records. Statistical analysis was performed using SPSS software to analyse and compare the baseline data of the two groups, calculate the changes in UACR, blood potassium, and eGFR in the treatment groups, and compare the differences between the groups. It was considered statistically significant when $p<0.05$.