Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Effect and Safety of Finerenone in Patients with IgA Nephropathy

Yanhong Guo*, Xuewen Zhang*, Silu Zhao*, Yulin Wang, Liuwei Wang, Qiuhong Li, Lu Yu, Lin Tang

Department of Nephropathy, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan, 450052, People's Republic of China

*These authors contributed equally to this work

Correspondence: Lin Tang, Department of Nephropathy, the First Affiliated Hospital of Zhengzhou University, No. 1 East Jianshe Road, Zhengzhou, Henan, 450052, People's Republic of China, Tel +8613838194409, Email tanglin@zzu.edu.cn

Purpose: The study aimed to retrospectively evaluate the efficacy and safety of finerenone in patients diagnosed with IgA nephropathy.

Methods: 42 IgA nephropathy patients treated with finerenone combined with renin–angiotensin system inhibitor (RASI) and 42 patients who received RASI monotherapy were included in this study. The follow-up duration was 3 months. The efficacy and safety of finerenone were assessed based on key parameters, including urine protein creatinine ratio (UPCR), estimated glomerular filtration rate (eGFR), serum creatinine, serum albumin, hematuria, and serum potassium at 1 and 3 months after treatment initiation.

Results: This study demonstrated that finerenone combined with RASI significantly reduced proteinuria in IgA nephropathy patients. Two-way repeated measures ANOVA revealed a significant time * treatment interaction ($P = 0.032$), and subsequent one-way repeated measures ANOVA showed a marked decline in log-transformed UPCR over time in the combination group ($P < 0.001$) but not in the monotherapy group ($P = 0.187$). Correspondingly, the combination group achieved a 27.29% reduction in UPCR at one month (95% CI: 13.47–39.68%, $P = 0.017$) and a 34.17% reduction at three months (95% CI: 21.84–52.75%, $P < 0.001$) compared to baseline, whereas RASI monotherapy failed to show any significant proteinuria-reduction effects. Notably, the antiproteinuric effect was consistent across subgroups. Serum potassium and creatinine levels remained stable, and no adverse events related to hyperkalemia were observed.

Conclusion: The retrospective evaluation suggests that finerenone combined with RASI effectively reduced proteinuria in IgA nephropathy patients, underscoring its potential as a viable treatment option for this patient population.

Keywords: finerenone, renin–angiotensin system inhibitor, IgA nephropathy, urine protein creatinine ratio

Introduction

As one of the most prevalent primary glomerular diseases in the world, IgA nephropathy is especially prevalent in China and East Asia.[1,2] IgA immunoglobulin deposition in the kidney, which causes mesangial proliferation, is the primary pathological symptom of IgA nephropathy. The most common clinical symptom of IgA nephropathy is hematuria, which is often accompanied by different levels of proteinuria or hypertension.[3]

Previous studies have generally suggested that only about one-third of IgA nephropathy patients progress to end-stage kidney disease (ESKD) 10–20 years after onset.[4] However, data from the UK's National Rare Kidney Disease Registry in 2023 indicate that based on existing treatment strategies, 50% of IgA nephropathy patients will develop ESKD or die within 10–15 years, and the vast majority will experience kidney failure during their lifetime. Even among those patients previously considered at low risk of kidney disease progression, up to 30% will still progress to ESKD within 10 years.[5] A recent cohort study analyzing the long-term prognosis of IgA nephropathy patients in China revealed that 22% of patients with well controlled urinary protein (0.5–1 g/d) developed renal failure within 10 years, while those with persistent urinary protein levels exceeding 1 g/d had a 10-year renal survival rate of only 36%.[6] The above studies suggest that under the current diagnostic and treatment paradigm, the prognosis of IgA nephropathy patients is

Received: 5 May 2025
Accepted: 9 July 2025
Published: 23 July 2025

significantly worse than previously widely believed. Consequently, there is an urgent need for new therapeutic agents and updated treatment strategies for IgA nephropathy.

The mineralocorticoid receptor (MR) is a key hormone receptor in the nucleus of the cell, widely present in various types of tissue such as the gastrointestinal tract, heart, brain, kidney, immune cells, and blood vessels, playing crucial physiological and pathological roles.[7,8] A small sample study has confirmed that the traditional steroid MR antagonist spironolactone can reduce proteinuria in IgA nephropathy.[9] However, spironolactone has not been extensively explored in the field of chronic kidney disease due to the risk of sex steroid receptor cross reactivity and hyperkalemia. Compared to traditional steroid MR antagonist, finerenone does not bind to glucocorticoid receptors, androgen receptors, and progesterone receptors, resulting in higher selectivity. Finerenone could act on the MR of glomeruli and renal tubules directly and comprehensively, exerting more potent anti-inflammatory and anti-fibrosis effects. This mechanism helps reduce glomerular hypertension and hyperfiltration, decrease urinary protein, and slow the progression of kidney disease.[10–12] Finerenone is predominantly used to treat patients with diabetic kidney disease. However, given its mechanism of action and proven efficacy in reducing proteinuria, its potential role in IgA nephropathy should not be overlooked. The objective of this study is to assess the safety and efficacy of finerenone in patients with IgA nephropathy, as current evidence on this therapeutic approach remains limited.

Materials and Methods

Study Design and Patients

This retrospective study, conducted at the First Affiliated Hospital of Zhengzhou University, initially identified 243 patients with biopsy-confirmed IgA nephropathy between January 2024 and May 2025 (Figure 1). Inclusion criteria were as follows: (1) age 18-80 years; (2) urinary protein excretion ≥0.5 g/d and eGFR ≥25 mL/min/1.73m^2; (3) diagnosis of

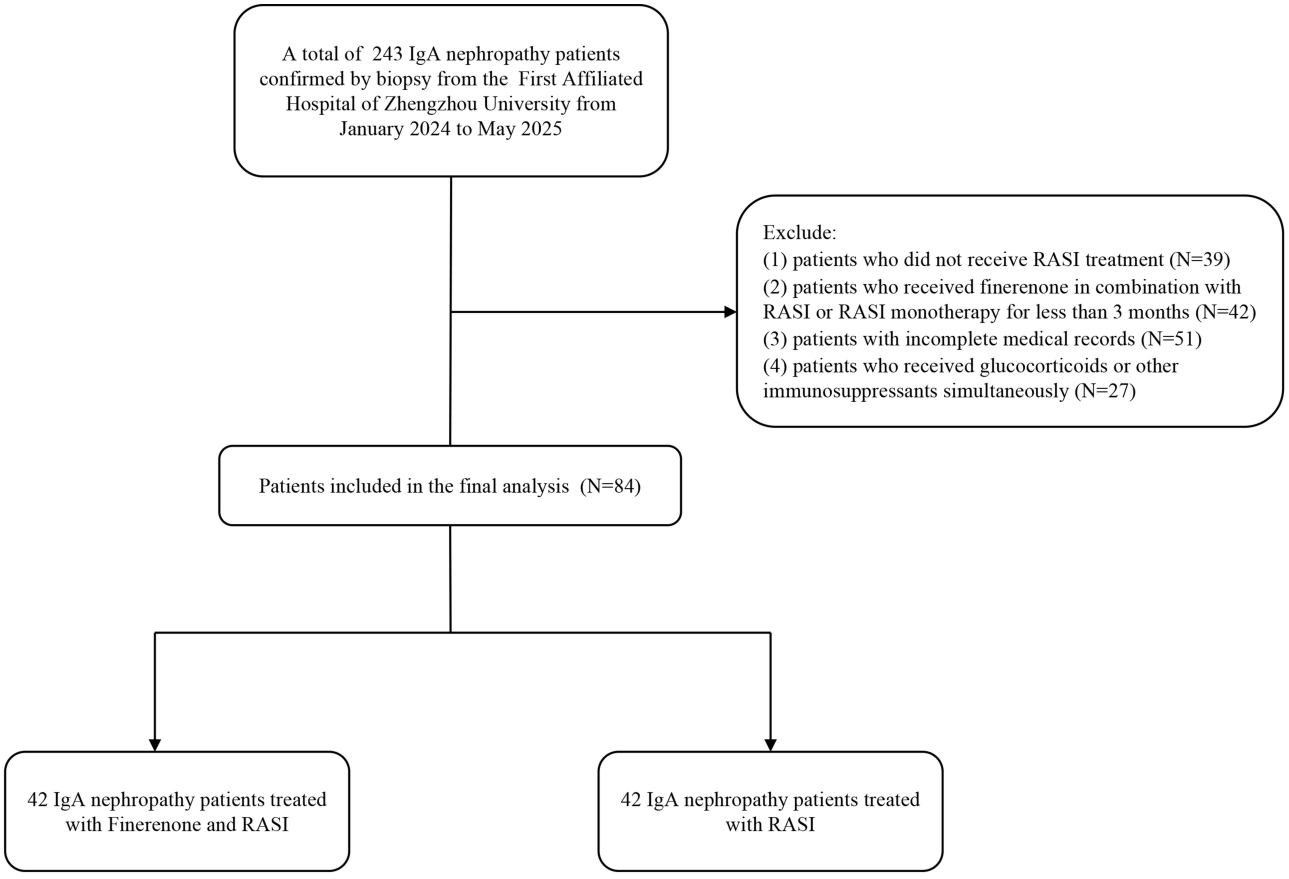

Figure 1 Flow chart of the study. RASI, renin–angiotensin system inhibitor.

IgA nephropathy was confirmed by renal biopsy; (4) treatment with finerenone combined with RASI or RASI monotherapy for more than three months. After excluding patients who (1) did not receive RASI treatment, (2) received finerenone plus RASI or RASI monotherapy for less than 3 months, (3) had incomplete medical records, or (4) received glucocorticoids or other immunosuppressants simultaneously, 84 eligible patients were stratified into two groups based on treatment regimen: the RASI plus finerenone group (n=42) and the RASI group (n=42). Notably, patients using sodium-dependent glucose transporters 2 inhibitor (SGLT2i) during the follow-up period were still included. The study was conducted in accordance with the Declaration of Helsinki Guidelines and received approval from the medical ethics committee of the First Affiliated Hospital of Zhengzhou University. All participants provided informed consent. They were informed of the use of their medical records for research purposes and were provided with the option to withdraw their consent.

Treatment Strategy

The starting dose of finerenone was based on eGFR. The recommended initial dose of finerenone is 20 mg once daily if the eGFR is higher than 60 mL/min/1.73 m^2. Starting with a dose of 10 mg once daily is advised if eGFR is between 25 and 60 mL/min/1.73m^2. In the RASI group, patients maintained the maximum recommended doses without titration throughout follow-up. During the follow-up, serum potassium was monitored and the dosage was adjusted according to the level of serum potassium within 4 weeks after starting the treatment of finerenone.

Data Collection

General clinical information, such as gender, age, blood pressure, body mass index (BMI), and previous medication regimens, was obtained from medical records. Laboratory parameters, including urine protein creatinine ratio (UPCR), eGFR, serum creatinine, serum albumin, hematuria, and serum potassium were recorded before the initiation of treatment and subsequently reassessed at one-month and three-month intervals following its administration. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) algorithm, which incorporates age, gender, race, and serum creatinine levels.

Statistical Analysis

Statistical analysis was performed using SPSS 27.0 software. The normality of continuous variables was assessed using the Shapiro–Wilk normality test. Continuous variables with normal distribution were presented as mean ± standard deviation, while non-normally distributed data were expressed as median and interquartile range (IQR). Between-group comparisons were conducted using the independent-samples *t*-test or the Mann–Whitney *U*-test, and within-group comparisons were performed using the paired *t*-test or the Wilcoxon signed-rank test. Categorical variables are presented as counts (percentages) and compared using the chi-square test or Fisher's exact test, as appropriate. For repeated measures data, normality at each time point was assessed using the Shapiro–Wilk test, and homogeneity of variances was tested using Levene's test. Non-normally distributed data were log-transformed prior to analysis. When assumptions were met, two-way repeated measures ANOVA was conducted. Sphericity was assessed using Mauchly's test; if violated, the Greenhouse–Geisser correction was applied. In cases of significant time * treatment interaction, simple effects were analyzed; otherwise, main effects were interpreted. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant. To control the type I error rate arising from multiple comparisons, Bonferroni correction was applied separately to the analyses of original values and percentage changes. Each correction set comprised six comparisons in total: within-group comparisons at 1 month and 3 months versus baseline in each group, and between-group comparisons at both time points. The adjusted significance level was therefore set at $\alpha' = 0.05/6 \approx 0.0083$.

Results

Characteristics of Study Population

In this study, 42 IgA nephropathy patients treated with finerenone combined with RASI were recruited as the study group, and 42 patients who received RASI monotherapy were enrolled as the control group. Table 1 outlines the baseline

Table 1 Characteristics of IgA Nephropathy Patients at Baseline

Characteristics	RASI + Finerenone (n=42)	RASI (n=42)	*P* Value
Age, years	38.71 ± 9.37	40.81 ± 12.52	0.388
Gender, male/female	15/27	22/20	0.124
BMI, kg/m^2	24.36 ± 2.63	24.93 ± 3.09	0.373
History of diabetes mellitus, n (%)	4 (9.52)	2 (4.70)	0.676
History of hypertension, n (%)	18 (42.86)	23 (54.76)	0.275
Systolic blood pressure, mmHg	125.26 ± 11.60	129.62 ± 12.34	0.099
Diastolic blood pressure, mmHg	79.79 ± 9.51	82.00 ± 8.83	0.272
Urinary protein excretion, g/d	1.22 (0.64, 2.04)	1.12 (0.65, 2.12)	0.802
Serum albumin, g/L	39.71 ± 5.15	39.26 ± 4.33	0.666
Serum creatinine, μmol/L	89.50 (66.75, 126.75)	102.00 (77.00, 128.00)	0.314
Serum potassium (mmol/L)	4.25 ± 0.37	4.37 ± 0.33	0.125
Hematuria, RBCs/μL	12.00 (3.00, 53.25)	10.50 (1.00, 20.00)	0.173
eGFR, mL/min per 1.73m²	77.04 ± 27.46	73.60 ± 29.12	0.579
eGFR category, n (%)			
≥90 mL/min per 1.73m²	14 (33.33)	12 (28.57)	0.826
≥60 to <90 mL/min per 1.73m²	14 (33.33)	17 (40.48)	
≥45 to <60 mL/min per 1.73m²	8 (19.05)	6 (14.29)	
≥30 to <45 mL/min per 1.73m²	5 (11.90)	6 (14.29)	
≥15 to <30 mL/min per 1.73m²	1 (2.38)	1 (2.38)	
Oxford classification			
M0/M1	25/17	20/22	0.274
E0/E1	20/22	26/16	0.188
S0/S1	8/34	12/30	0.306
T0/T1/T2	26/8/8	26/9/7	0.934
C0/C1/C2	18/21/3	22/18/2	0.366
Concomitant medications, n (%)			
SGLT2 inhibitor	16 (38.10)	10 (23.81)	0.157

Notes: Data are presented as n (%), mean ± SD or median (IQR). eGFR was determined using the Chronic Kidney Disease Epidemiology formula. The Oxford classification was developed by the Working Group of the International IgA Nephropathy Network and the Renal Pathology Society.

Abbreviations: BMI, body mass index; RASI, renin–angiotensin system inhibitor; RBC, red blood cell; SGLT2, sodium-dependent glucose transporters 2; eGFR, estimated glomerular filtration rate.

characteristics of the study population. There was no statistically significant difference between the two groups in general clinical information, including gender, age, blood pressure, BMI, and previous medication regimens. In addition, comparison of laboratory parameters, such as UPCR, eGFR, serum creatinine, serum albumin, hematuria, and serum potassium between the two groups showed no significant difference at baseline.

Comparison of Proteinuria Reduction Between RASI Plus Finerenone Therapy and RASI Monotherapy

As shown in Tables 2 and 3, two-way repeated measures ANOVA revealed a significant time * treatment interaction (F = 3.508, P = 0.032), suggesting that the pattern of UPCR changes over time varied according to treatment modality. A significant time effect on log-transformed UPCR was also observed (F = 13.527, P < 0.001), indicating a significant overall change in UPCR levels across the study period. Notably, the treatment effect was not statistically significant (F = 0.542, P = 0.464), indicating no significant overall difference in UPCR levels between the two groups, which does not contradict the significant interaction effect. No significant effects of time, treatment and time * treatment interaction were observed for eGFR, serum creatinine, serum albumin, hematuria, or serum potassium, suggesting that these parameters remained stable throughout the study and showed no significant changes related to treatment modality.

Given the significant interaction effect, we focused on the interaction effect rather than the main effect and conducted separate one-way repeated measures ANOVA for each group. A significant reduction in log-transformed UPCR over time

Table 2 Repeated Measures Analysis of Clinical Characteristics in the Two Groups During Treatment

Variables	Time			*P* Value		
	Baseline	1 Month	3 Months	Time	Treatment	Time * Treatment
UPCR, g/g						
RASI + Finerenone	1.22 (0.64, 2.04)	0.86 (0.45, 1.83)	0.68 (0.34, 1.50)	<0.001	0.464	0.032
RASI	1.12 (0.65, 2.12)	0.91 (0.69, 1.84)	1.04 (0.57, 1.50)			
eGFR, mL/min per 1.73m²						
RASI + Finerenone	77.04 ± 27.46	77.38 ± 27.44	75.94 ± 27.40	0.560	0.650	0.730
RASI	73.60 ± 29.12	74.49 ± 29.22	73.91 ± 30.54			
Serum albumin, g/L						
RASI + Finerenone	39.71 ± 5.15	40.17 ± 5.23	41.49 ± 7.03	0.206	0.159	0.155
RASI	39.26 ± 4.33	38.91 ± 4.68	39.09 ± 3.97			
Serum creatinine, μmol/L						
RASI + Finerenone	89.50 (66.75, 126.75)	92.00 (67.75,131.00)	91.00 (69.75, 132.50)	0.410	0.426	0.566
RASI	102.00 (77.00, 128.00)	101.50 (71.00,128.75)	102.00 (72.00, 136.25)			
Serum potassium, mmol/L						
RASI + Finerenone	4.22 (4.01, 4.47)	4.31 (3.95, 4.49)	4.29 (3.92, 4.54)	0.885	0.379	0.288
RASI	4.38 (4.11, 4.54)	4.27 (4.05, 4.61)	4.22 (3.94, 4.60)			
Hematuria, RBCs/μL						
RASI + Finerenone	12.00 (3.00, 53.25)	8.50 (2.00, 24.25)	6.00 (0.75, 32.00)	0.998	0.592	0.275
RASI	10.50 (1.00, 20.00)	10.50 (6.00, 8.50)	8.50 (2.00, 27.25)			

Notes: Data are presented as mean ± SD or median (IQR). All data were analyzed using repeated measures ANOVA, with non-normally distributed data log-transformed to normally distributed data. eGFR was determined using the Chronic Kidney Disease Epidemiology formula.
Abbreviations: UPCR, urine protein creatinine ratio; RASI, renin–angiotensin system inhibitor; RBC, red blood cell; eGFR, estimated glomerular filtration rate.

Table 3 Comparison of UPCR Between the Two Groups During Treatment

Group	Baseline	1 Month	3 Months	F	*P* Value
RASI + Finerenone	1.22 (0.64, 2.04)	0.86 (0.45, 1.83) **	0.68 (0.34, 1.50) ***	14.895	<0.001
RASI	1.12 (0.65, 2.12)	0.91 (0.69, 1.84)	1.04 (0.57, 1.50)	1.709	0.187
U	0.002	4.092	6.336		
P value	0.804	0.453	0.163		
	F (Time) =13.527 F (Treatment) = 0.542 F (Time * Treatment) = 3.508 *P* (Time) < 0.001 *P* (Treatment) = 0.464 *P* (Time * Treatment) = 0.032				

Notes: Data are presented as median (IQR). ** and *** indicate significant differences compared with baseline data ($P < 0.01$ and $P < 0.001$, respectively).
Abbreviations: UPCR, Urine protein creatinine ratio; RASI, renin–angiotensin system inhibitor.

was observed in the RASI + finerenone group ($F = 14.895$, $P < 0.001$), while no significant change was found in the RASI monotherapy group ($F = 1.709$, $P = 0.187$). Correspondingly, the RASI + finerenone group achieved significant reductions in UPCR from baseline to both 1 month [0.86 (0.45, 1.83) vs 1.22 (0.64, 2.04) g/g, $P = 0.003$] and 3 months [0.68 (0.34, 1.50) vs 1.22 (0.64, 2.04) g/g, $P = 0.001$], whereas the RASI monotherapy group maintained stable UPCR levels throughout the study period with no significant changes observed at either the 1 month or 3 months timepoints when compared to baseline level ($P > \alpha'$). Notably, between-group comparisons of UPCR at 1 month, and 3 months revealed no statistically significant differences ($P = 0.453$, and 0.163, respectively), as detailed in Table 3.

As illustrated in Figure 2, treatment with RASI + finerenone resulted in a sustained and consistent decrease in proteinuria among IgA nephropathy patients. After one month of therapy, a notable reduction in proteinuria of 27.29% [95% confidence interval (CI), 13.47–39.68%, P =0.017] was observed compared to baseline. At the three-month visit, the reduction reached 34.17% (95% CI, 21.84–52.75%; $P < 0.001$), showing statistically significant improvement. In the RASI monotherapy group, UPCR levels showed a non-significant downward trend, with reductions of 8.29% (95% CI, −0.77–17.81%; $P = 0.389$) at one month and 12.24% (95% CI, −4.28–22.00%; $P = 0.112$) at three months post-treatment,

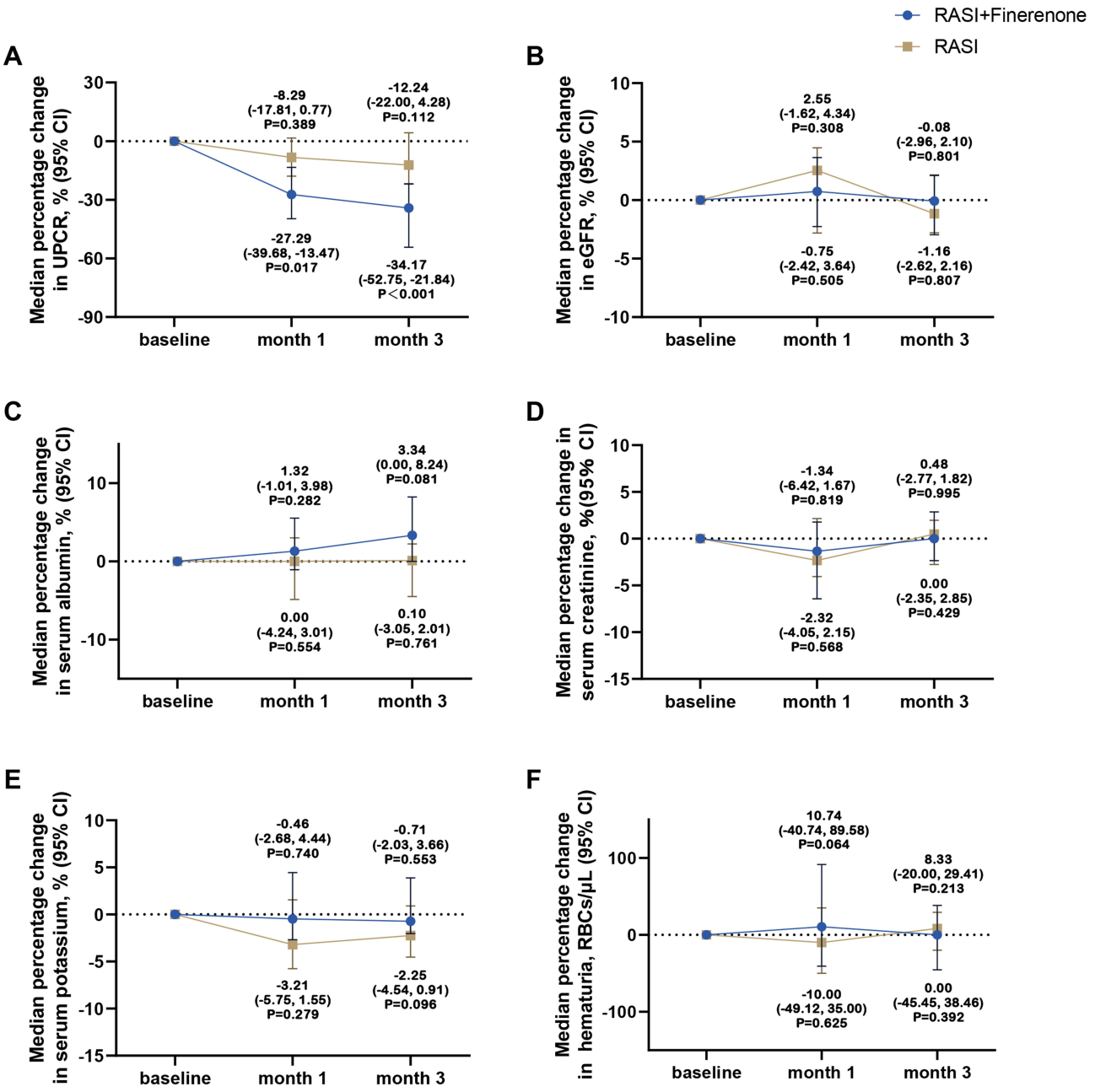

Figure 2 Median percentage changes in (**A**) UPCR, (**B**) eGFR, (**C**) serum albumin, (**D**) serum creatinine, (**E**) serum potassium, and (**F**) hematuria over 3 months of treatment in the RASI + Finerenone and RASI groups. Data are presented as median (95% CI). *P values* represent the comparison of median percentage changes in UPCR from baseline to different follow-up time points in the two groups. eGFR was determined using the Chronic Kidney Disease Epidemiology formula.

Abbreviations: RASI, renin–angiotensin system inhibitor; CI, confidence interval; UPCR, urine protein creatinine ratio; RBC, red blood cell; eGFR, estimated glomerular filtration rate.

indicating a potential but statistically unconfirmed treatment effect on proteinuria reduction. Table 4 demonstrates that after 3 months of treatment, the RASI + finerenone group achieved a significantly greater reduction in UPCR [−34.17 (−65.99, −2.32) vs −12.23 (−34.55, 10.31) %, *P*=0.007)] compared to the RASI monotherapy group, supporting the superior proteinuria-reducing efficacy of combination therapy over RASI alone.

Table 4 demonstrates that significantly more patients in the RASI + finerenone group achieved clinically meaningful UPCR reductions compared to the RASI monotherapy group. At one month, 19 patients (45.24%) versus 8 (19.05%) attained ≥30% reduction (*P*=0.010), and 12 (28.57%) versus 4 (9.52%) reached ≥50% reduction (*P*=0.026). By three months, further improvements were observed: 25 patients (59.52%) versus 9 (21.43%) achieved ≥30% reduction

Table 4 Changes in Clinical Characteristics During Treatment

Variables	1 Month	*P* Value	3 Months	*P* Value
Percentage change in UPCR (%)				
RASI + Finerenone	−27.29 (−54.63, −1.69)	0.105	−34.17 (−65.99, −2.32)	0.007
RASI	−8.29 (−33.01, 23.26)		−12.23 (−34.55, 10.31)	
Patients with ≥30% reduction in UPCR, n (%)				
RASI + Finerenone	19 (45.24)	0.010	25 (59.52)	<0.001
RASI	8 (19.05)		9 (21.43)	
Patients with ≥50% reduction in UPCR, n (%)				
RASI + Finerenone	12 (28.57)	0.026	16 (38.10)	0.006
RASI	4 (9.52)		5 (11.90)	
Percentage change in eGFR (%)				
RASI + Finerenone	0.75 (−6.75, 8.12)	0.788	−0.08 (−7.79, 6.42)	0.922
RASI	2.55 (−4.57, 8.85)		−1.16 (−4.85, 5.14)	
Percentage change in serum albumin (%)				
RASI + Finerenone	1.32 (−2.01, 6.74)	0.287	3.34 (−5.05, 10.75)	0.123
RASI	0.00 (−6.50, 5.45)		0.10 (−6.30, 4.07)	
Percentage change in serum creatinine (%)				
RASI + Finerenone	−1.34 (−9.23, 8.78)	0.964	0.00 (−6.67, 9.64)	0.730
RASI	−2.32 (−7.27, 4.85)		0.48 (−6.82, 8.57)	
Percentage change in serum potassium (%)				
RASI + Finerenone	−0.46 (−6.02, 7.31)	0.291	−0.71 (−5.57, 9.73)	0.128
RASI	−3.21 (−6.89, 4.60)		−2.25 (−7.56, 2.36)	
Percentage change in hematuria (%)				
RASI + Finerenone	10.74 (−63.88, 100.00)	0.548	0.00 (−81.18, 100.00)	0.577
RASI	−10.00 (−95.45, 107.50)		8.33 (−33.64, 82.50)	

Notes: Data are presented as n (%) or median (IQR). eGFR was determined using the Chronic Kidney Disease Epidemiology formula. Percentage change = (Follow-up data - Baseline data) / Baseline data * 100.

Abbreviations: UPCR, urine protein creatinine ratio; RASI, renin–angiotensin system inhibitor; RBC, red blood cell; eGFR, estimated glomerular filtration rate.

(*P*<0.001), and 16 (38.10%) versus 5 (11.90%) attained ≥50% reduction (*P*=0.006). These results collectively demonstrate the superior efficacy of combination therapy in achieving substantial proteinuria reduction targets at both time points.

Subgroup Analysis of Finerenone's Effect on Proteinuria Reduction

As shown in Figure 3, the subgroup analysis indicated that the effect of finerenone on reducing proteinuria at both one-month and three-month intervals was consistent and did not show significant differences across different baseline factors. These factors include baseline age (≥38 years or <38 years, *P*=0.379 for one month and *P*=0.421 for three months), gender (male or female, *P*=0.783 for one month and *P*=0.763 for three months), BMI (≥24 kg/m^2 or <24 kg/m^2, *P*=0.889 for one month and *P*=0.714 for three months), status of hypertension (*P*=0.501 for one month and *P*=0.809 for three months), status of diabetes (*P*=0.695 for one month and *P*=0.885 for three months), baseline serum creatinine (≥89 μmol/L or <89 μmol/L, *P*=0.695 for one month and *P*=0.604 for three months), baseline eGFR (≥77 mL/min/1.73m^2 or <77 mL/min/1.73m^2, *P*=0.714 for one month and *P*=0.370 for three months), proteinuria (≥1.22 g/L or <1.22 g/L, *P*=0.919 for one month and *P*=0.780 for three months), hematuria (≥12/μL or <12/μL, *P*=0.521 for one month and *P*=0.782 for three months), the use of SGLT2i (*P*=0.249 for one month and *P*=0.959 for three months).

Safety of Finerenone for IgA Nephropathy Patients

Throughout the study period, serum potassium levels remained stable in both groups, with no significant changes over time or between the two groups (Table 2). Additionally, as shown in Figure 2, the percentage change in serum potassium from baseline was not statistically significant at any time point in either group. Importantly, no treatment discontinuations

https://doi.org/10.2147/JIR.S531236

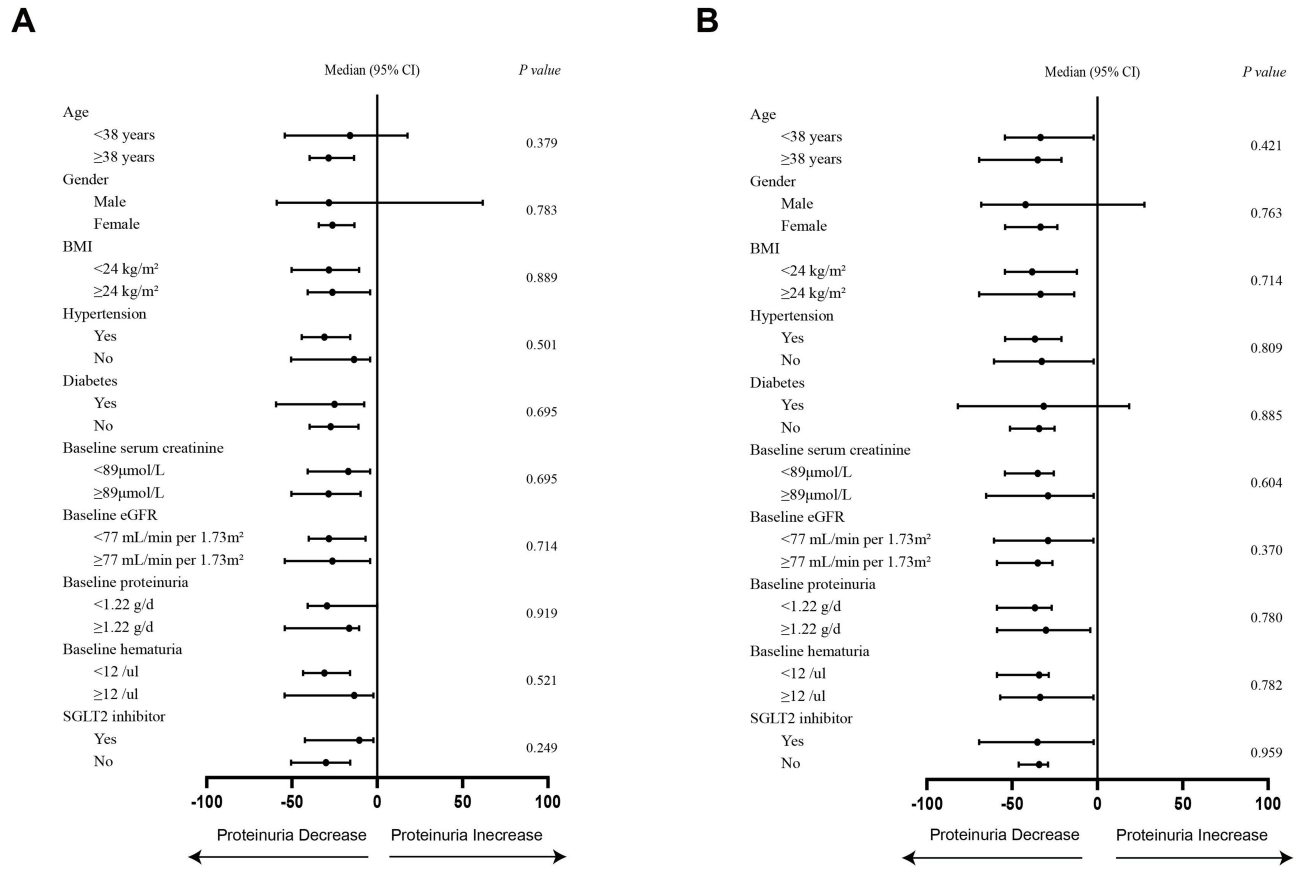

Figure 3 Subgroup analysis of finerenone combined with RASI on proteinuria reduction at one month (**A**) and at three months (**B**). Data are presented as median (95% CI). eGFR was determined using the Chronic Kidney Disease Epidemiology formula.
Abbreviations: CI, confidence interval; BMI, body mass index; SGLT2, sodium-dependent glucose transporters 2; eGFR, estimated glomerular filtration rate.

or hospitalizations related to hyperkalemia occurred during the study period, indicating a safe and stable potassium balance during treatment.

Discussion

IgA nephropathy, the most prevalent primary glomerular disease worldwide, is also one of the most common causes of ESKD.[13] Patients of IgA nephropathy have a dismal prognosis, and even patients with microalbuminuria, which is traditionally considered to have a low progression risk, may still have a high risk of renal failure. Current therapeutic approaches fall well short of clinical requirements.[1] The recent development and application of a large number of new therapeutic drugs are expected to improve the current situation, and the treatment strategy will also shift towards a comprehensive multi-target treatment strategy.[14–19] The future will be an important opportunity period for the rapid development of IgA nephropathy treatment. The "Four-Hit Hypothesis" is currently widely accepted as the pathogenesis of IgA nephropathy on a global scale.[20] Based on the widely recognized pathological mechanism of the "Four-Hit Hypothesis", new breakthroughs have been made in different targeted drugs. The fourth hit is the deposition of immune complexes in renal mesangial cells, activating complement and other mediators, leading to inflammation, glomerulosclerosis, and progressive renal injury with interstitial fibrosis.

Finerenone is a highly selective nonsteroidal mineralocorticoid receptor antagonist, which is mainly used to treat patients with chronic kidney disease and type 2 diabetes.[21] Finerenone inhibits the activation of downstream signaling pathways by binding to MR and blocking the binding of aldosterone to MR, thereby reducing the infiltration of inflammatory cells and the expression of fibrosis related genes, exerting anti-inflammatory and anti-fibrotic effects.[22] Finerenone exert anti-inflammatory effects in the kidney and heart, which is mediated through the selective inhibition

of the MR. Finerenone can also exert anti-inflammatory effects by shifting the M1 macrophage phenotype, which promotes inflammation, to the M2 phenotype, known for its anti-inflammatory properties because of changes in gene expression through the MR in macrophages.[23] Secondly, finerenone can reduce oxidative stress levels, improve endothelial function, and decrease superoxide anion levels.[24,25] For renal diseases, finerenone can reduce renal inflammatory cell infiltration, decrease the expression and release of inflammatory factors, and alleviate renal inflammatory damage.[26,27] At the same time, inhibiting renal interstitial fibrosis and reducing collagen synthesis by finerenone can help maintain glomerular filtration rate, reduce proteinuria, and delay the progression of chronic kidney disease.[22] It is precisely because of the powerful anti-inflammatory, anti-fibrotic, and hemodynamic mechanisms of finerenone that it provides a theoretical basis for its application in IgA nephropathy, especially the kidney inflammation and fibrosis caused by "the fourth hit".

This is the first study on the efficacy and safety of finerenone combined with RASI in patients with IgA nephropathy, and there have been no previous related studies. In our analysis of 84 patients with IgA nephropathy, finerenone combined with RASI demonstrated significant therapeutic potential, evidenced by a notable reduction in UPCR and consistent eGFR values throughout the treatment duration. Another key aspect of this study is the safety of finerenone combined with RASI in IgA nephropathy patients. Serum potassium levels remained stable during the treatment period, with no instances of treatment discontinuation or hospitalization due to hyperkalemia, underscoring finerenone's lower risk of inducing elevated potassium levels. Notably, these outcomes were consistent across diverse factors such as age, gender, BMI, presence of diabetes or hypertension, baseline serum creatinine, baseline eGFR, proteinuria, hematuria, and the use of SGLT2 inhibitors. Our research contributes to important clinical data in favor of the application of finerenone in IgA nephropathy by offering limited but insightful information about the efficacy and safety of finerenone in these patients.

While our study provides important insights into the effect of finerenone combined with RASI in IgA nephropathy patients, some limitations should be considered when interpreting the findings. First, it is a retrospective analysis, which provides a lower level of evidence compared to randomized controlled study. Second, the sample size included in this research is relatively small. Third, the duration of follow-up was comparatively brief. As a result, future randomized controlled trials with larger patient cohorts are needed to further validate the long-term impact of finerenone on proteinuria and renal function in individuals with IgA nephropathy.

Conclusion

In conclusion, finerenone combined with RASI has demonstrated a certain efficacy in lowering proteinuria in patients with IgA nephropathy. Regardless of age, gender, BMI, diabetes, hypertension, baseline serum creatinine, baseline eGFR, proteinuria, hematuria, and the use of SGLT2i, this effect is still substantial. The long-term renal protective effect of finerenone on patients with IgA nephropathy requires more investigation.

Data Sharing Statement

Data can be obtained upon request to the corresponding author.

Ethics Approval

The study was approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University.

Informed Consent

Informed consent was derived from the participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China (grant no. 82200839 and 82370727).

Disclosure

The authors declare that there is no conflict of interest in this work.

References

1. Pattrapornpisut P, Avila-Casado C, Reich HN. IgA Nephropathy: core Curriculum 2021. *Am J Kidney Dis*. 2021;78(3):429–441. doi:10.1053/j.ajkd.2021.01.024
2. Zaidi O, Du F, Tang Z, Bhattacharjee S, Pareja K. Review on epidemiology, disease burden, and treatment patterns of IgA nephropathy in select APAC countries. *BMC Nephrol*. 2024;25(1):136. doi:10.1186/s12882-024-03555-5
3. Disease K. Improving Global Outcomes Glomerular Diseases Work G. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int*. 2021;100(4S):S1–S276. doi:10.1016/j.kint.2021.05.021
4. Robert JW, Bruce AJ. IgA nephropathy. *N Engl J Med*. 2013;368(25):2402–2414. doi:10.1056/NEJMra1206793
5. David P, Fiona B, Bruce H, et al. Long-Term Outcomes in IgA Nephropathy. *Clin J Am Soc Nephrol*. 2023;18(6):727–738. doi:10.2215/cjn.0000000000000135
6. Chen T, Pei C, Feng-Lei S, et al. Time-Varying Proteinuria and Progression of IgA Nephropathy: a Cohort Study. *Am J Kidney Dis*. 2024;84(2):170–178. doi:10.1053/j.ajkd.2023.12.016
7. J F, F N. Emerging Roles of the Mineralocorticoid Receptor in Pathology: toward New Paradigms in Clinical Pharmacology. *Pharmacol Rev*. 2015;68(1):49–75. doi:10.1124/pr.115.011106
8. Peter K, Amer J, Ulrich K. Nonsteroidal mineralocorticoid receptor antagonism for cardiovascular and renal disorders - New perspectives for combination therapy. *Pharmacol Res*. 2021;172:49–75. doi:10.1016/j.phrs.2021.105859
9. Shang D, Guan Y, Liu S, Hao C, Lai L. Effectiveness and Safety of Spironolactone in the Treatment of IgA Nephropathy: a Retrospective Self-Controlled Study. *Kidney Blood Pressure Res*. 2024;49(1):687–698. doi:10.1159/000540283
10. Ruiz-Hurtado G, Ruilope L. Cardiorenal protection during chronic renin-angiotensin-aldosterone system suppression: evidences and caveats. *Eur Heart J Cardiovasc Pharmacother*. 2015;1(2):126–131. doi:10.1093/ehjcvp/pvu023
11. Zelniker T, Braunwald E. Mechanisms of Cardiorenal Effects of Sodium-Glucose Cotransporter 2 Inhibitors: JACC State-of-the-Art Review. *J Am College Cardiol*. 2020;75(4):422–434. doi:10.1016/j.jacc.2019.11.031
12. González-Juanatey J, Valle A, Valle A, Soler M, Facila L, Facila L. Cardiorenal benefits of finerenone: protecting kidney and heart. *Annal Med*. 2023;55(1):502–513. doi:10.1080/07853890.2023.2171110
13. Jennifer CR, Mark H, Heather NR. IgA Nephropathy. *Clin J Am Soc Nephrol*. 2017;12(4):677. doi:10.2215/cjn.07420716
14. Hiddo JLH, Meg J, Donald EK, et al. Atrasentan in Patients with IgA Nephropathy. *N Engl J Med*. 2024;392:544–554. doi:10.1056/NEJMoa2409415
15. Vlado P, Jonathan B, Brad R, et al. Alternative Complement Pathway Inhibition with Iptacopan in IgA Nephropathy. *N Engl J Med*. 2024;392:531–543. doi:10.1056/NEJMoa2410316
16. Julie RI. Way Stations in Progress - Burgeoning Treatment Options for IgA Nephropathy. *N Engl J Med*. 2024;392:608–609. doi:10.1056/NEJMe2413288
17. Yonghua Z, Xin D, Jianjun Z. Targeted release of budesonide in primary IgA nephropathy. *Lancet*. 2024;403(10446):2785. doi:10.1016/s0140-6736(24)00795-5
18. Mohit M, Jonathan B, Yusuke S. Phase 2 Trial of Sibeprenlimab in Patients with IgA Nephropathy. Reply. *N Engl J Med*. 2024;390(13):1245. doi:10.1056/NEJMc2401277
19. Kevin VL, Richard JG. April - Springtime for New IgA Nephropathy Therapy? *N Engl J Med*. 2024;390(1):80. doi:10.1056/NEJMe2312300
20. Chee Kay C, Suceena A, Heather NR, Haresh S, Hong Z, Jonathan B. The pathogenesis of IgA nephropathy and implications for treatment. *Nat Rev Nephrol*. 2024;21(1):9–23. doi:10.1038/s41581-024-00885-3
21. George LB, Rajiv A, Stefan DA, et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. *N Engl J Med*. 2020;383(23):2219. doi:10.1056/NEJMoa2025845
22. Karoline D, Mira P, Manuel G, et al. Direct Blood Pressure-Independent Anti-Fibrotic Effects by the Selective Nonsteroidal Mineralocorticoid Receptor Antagonist Finerenone in Progressive Models of Kidney Fibrosis. *Am J Nephrol*. 2021;52(7):588–601. doi:10.1159/000518254
23. Jonatan B-C, Gabriel RE, Sebastian ML, et al. The myeloid mineralocorticoid receptor controls inflammatory and fibrotic responses after renal injury via macrophage interleukin-4 receptor signaling. *Kidney Int*. 2018;93(6):1344. doi:10.1016/j.kint.2017.12.016
24. Panagiotis T, Aikaterini V, Rigas GK. Oxidative Stress Management in Cardiorenal Diseases: focus on Novel Antidiabetic Agents, Finerenone, and Melatonin. *Life*. 2022;12(10):1663. doi:10.3390/life12101663
25. Raquel G-B, Beatriz S, Marta G-O, et al. Finerenone Attenuates Endothelial Dysfunction and Albuminuria in a Chronic Kidney Disease Model by a Reduction in Oxidative Stress. *Front Pharmacol*. 2018;9:1131. doi:10.3389/fphar.2018.01131
26. Ruimin Z, Qian W, Yaqing L, et al. A new perspective on proteinuria and drug therapy for diabetic kidney disease. *Front Pharmacol*. 2024;15:1349022. doi:10.3389/fphar.2024.1349022
27. Sandra R-M, Raul RR-D, Beatriz -F-F, et al. Targeting inflammation to treat diabetic kidney disease: the road to 2030. *Kidney Int*. 2022;103(2):282–296. doi:10.1016/j.kint.2022.10.030