DOI: 10.66069/ojspub.27450827

IgA Nephropathy: Research Status and Therapeutic Progress with Integrated Traditional Chinese and Western Medicine

Xianyi Huang[1], Yun Tian[2]

[1]First Clinical Medical College of Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China,
[2]Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, Shaanxi, China,
[1]huangxianyi1128@163.com, [2]doctortianyun@126.com
**Correspondence Author*

Abstract: ***Immunoglobulin A nephropathy (IgAN) is the most common primary glomerulonephritis worldwide and a leading cause of end-stage renal disease (ESRD). Epidemiological data indicate that China has approximately 4.59 million IgAN patients, with only 570,000 diagnosed, imposing a substantial economic burden. In recent years, with the establishment of the "four-hit" pathogenesis model and advances in gut mucosal immunity research, treatment strategies for IgAN have been shifting from traditional non-specific immunosuppression toward targeted and stratified therapies. In traditional Chinese medicine (TCM), diverse syndrome differentiation systems based on wind pathogen, kidney deficiency and blood stasis, damp-heat, and triple energizer theories have been developed, demonstrating unique value in symptom improvement, proteinuria reduction, and delaying renal function decline. In Western medicine, the 2025 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Management of IgAN—the first standalone guideline for this condition—proposes a paradigm shift toward "simultaneous initiation" of etiological intervention and complication management. Renin-angiotensin system (RAS) blockers and sodium-glucose cotransporter-2 (SGLT2) inhibitors are now recommended as first-line supportive therapies, while novel agents including complement inhibitors (iptacopan), dual endothelin angiotensin receptor antagonists (sparsentan, atrasentan), targeted-release budesonide (Nefecon), and BAFF/APRIL-targeted therapies (telitacicept, sibeprenlimab, etc.) continue to emerge, offering additional treatment options for IgAN. This article systematically reviews the latest advances in the epidemiology, pathogenesis, clinical classification, and integrated TCM-Western medicine treatment of IgAN, aiming to provide references for clinical practice and future research.***

Keywords: IgA nephropathy, Integrated traditional Chinese and Western medicine, Targeted therapy, KDIGO guideline.

1. Introduction

IgA nephropathy (IgAN) is the most common primary glomerulonephritis globally and a significant contributor to end-stage renal disease (ESRD). Epidemiological data indicate that patients with IgAN face a 26% risk of progressing to ESRD within ten years, with a global incidence of at least 2.5 per 100,000 population, accounting for approximately one-third of chronic glomerulonephritis cases [1]. According to Du et al., China has approximately 4.59 million IgAN patients, of whom only 570,000 are diagnosed; annual hospitalization costs range from RMB 4,867 to 14,900 per patient, and if the disease progresses to ESRD, annual dialysis costs amount to RMB 70,000-120,000 [2]. Based on the 2016 China Kidney Disease Network (CK-NET) Annual Data Report, approximately 600,000 patients receive dialysis treatment in China, with total medical expenditure exceeding RMB 50 billion [3]. IgAN has become a serious public health problem in China.

2. Current Research Status

2.1 Epidemiological Characteristics

IgAN demonstrates significant geographical and ethnic variations in incidence. It is most prevalent in East Asia, particularly in China, Japan, and Korea, where it accounts for 30-40% of primary glomerulonephritis cases diagnosed by renal biopsy. In Europe and North America, the proportion is lower, ranging from 10-20% [1]. The disease predominantly affects young adults, with a peak age of onset between 20 and 39 years, and shows a male predominance with a male-to-female ratio of approximately 2:1.

2.2 Pathogenesis

The pathogenesis of IgAN has not been fully elucidated, but the "four-hit" hypothesis has gained wide acceptance [4]. Hit 1: Genetic susceptibility leads to abnormal glycosylation of immunoglobulin A (IgA), producing galactose-deficient IgA1 (Gd-IgA1). The structural abnormality makes Gd-IgA1 more prone to aggregation and deposition in the mesangium. Hit 2: Production of specific antibodies against Gd-IgA1, predominantly immunoglobulin G (IgG) and, to a lesser extent, IgA1. These antibodies show 80% increased affinity for Gd-IgA1, though the mechanisms underlying this phenomenon remain unclear [4]. Hit 3: Formation of athogenic immune complexes containing Gd-IgA1. Studies indicate that Gd-IgA1 alone does not cause renal injury [5]; rather, Gd-IgA1 binds with IgG antibodies to form pathogenic immune complexes. Hit 4: Deposition of pathogenic immune complexes in the mesangium activates mesangial cells and triggers the complement system via the lectin or alternative pathways, inducing immune responses and local inflammation, ultimately leading to renal damage. The complement system plays a critical role in IgAN pathogenesis, offering potential new targets for treatment.

In addition to genetic factors, gut mucosal immunity and intestinal microbiota dysbiosis may contribute to IgAN onset or exacerbation. Genome-wide association studies have identified risk loci associated with maintaining intestinal mucosal integrity, providing evidence linking mucosal

immune abnormalities to IgAN [6]. Research demonstrates that IgAN patients exhibit gut microbiota dysbiosis, which impairs intestinal immune barrier function, allowing harmful metabolites and pathogens to invade the intestinal mucosa, triggering inflammatory responses and inducing Gd-IgA1 production [6].

2.3 Clinical Classification

Based on clinical manifestations, IgAN is classified into five types: (1) asymptomatic hematuria with or without mild proteinuria; (2) recurrent gross hematuria; (3) chronic nephritic syndrome; (4) nephrotic syndrome; and (5) acute kidney injury [4]. Type 1 generally requires no special treatment beyond regular follow-up and avoidance of fatigue and nephrotoxic drugs, with favorable prognosis. Type 2 typically presents following upper respiratory tract infections; the degree of gross hematuria does not correlate with disease severity, and after resolution, it often converts to type 1. For patients with chronic nephritic syndrome, symptomatic treatment with close blood pressure monitoring is recommended; RAS blockers should be administered even in normotensive patients to reduce proteinuria. Nephrotic syndrome, being more clinically apparent, warrants prompt renal biopsy for pathological clarification; patients with IgAN complicated by minimal change disease have a relatively favorable prognosis, while those with renal impairment have a poorer outlook. Acute kidney injury requires targeted intervention, particularly in cases of rapidly progressive glomerulonephritis.

3. Treatment Approaches

3.1 Traditional Chinese Medicine

The etiology and pathogenesis of IgAN are complex, with diverse clinical presentations. While different schools of thought exist, most practitioners recognize the condition as one of root deficiency with branch excess. The disease is located in the kidney; although it arises from deficiency of vital energy, it often leads to excess manifestations, generating damp-heat pathogenic factors that further exacerbate the condition. Clinically, treatment approaches are commonly based on wind pathogen, blood stasis, damp-heat, triple energizer, and deficiency-excess differentiation.

3.1.1 Treatment Based on Wind Pathogen Theory

Proponents of wind pathogen theory hold that exogenous wind is both the initial trigger and a cause of disease recurrence. However, the presence of internal wind should not be overlooked—prolonged illness depletes vital energy, generating internal wind that aggravates the condition.

Professor Lv Renhe proposed that patients develop kidney deficiency before wind pathogen can cause disease. Wind pathogen invades the zang-fu organs and meridians, transforming into various “wind toxins” [7]. If it affects fluid metabolism, edema develops; if renal collaterals are impaired, proteinuria and hematuria appear [8]. Professor Zhang Yu believes that wind gradually descends from the throat to the kidney, often lurking in the body and recurring upon exposure to external pathogens [9]. Professor Cao Shili adds that dampness often combines with wind, exacerbating the condition and prolonging its course [10].

In treatment, Professor Zhang Yu emphasizes the spleen and kidney, using large doses of Huangqi (Astragalus membranaceus)—up to 60-200g [11]—following the principle from Wenbing Tiaobian (Systematic Differentiation of Warm Diseases) that “treating the lower energizer requires weighty medicinals to reach the kidney and liver directly.” Different types of wind are treated differently: external wind should be dispersed, internal wind should be calmed, and latent wind should be treated according to warm disease latent pathogen principles, using the four methods of “warming, nourishing, penetrating, and clearing” to eliminate wind [12]. Professor Huang Wenzheng developed the Chan Can Shen Feng Tang (Cicada and Silkworm Kidney Wind Decoction), with cicada slough and bombyx batryticatus as sovereign herbs to dispel wind and detoxify; madder and suberect spatholobus stem as minister herbs to remove stasis and activate blood; motherwort and smilax glabra to resolve turbidity and drain dampness; and Chinese yam, white atractylodes, codonopsis, and licorice as assistant herbs to supplement qi and warm yang; with Chinese angelica, rehmannia, and raspberry to nourish yin and consolidate. This formula has demonstrated consistent therapeutic efficacy [13].

3.1.2 Treatment Based on Kidney Deficiency and Blood Stasis

The kidney deficiency and blood stasis theory was pioneered by Professor Zhang Daning, who posits that prolonged kidney disease invariably manifests as “kidney deficiency, blood stasis, and turbid toxin retention” [14]. Kidney deficiency inevitably involves blood stasis, which further exacerbates kidney deficiency, creating a vicious cycle [15]. Professor Yang Nizhi observed that spleen-kidney deficiency is the foundation of disease development; impairment of zang-fu transportation and transformation functions leads to blood stasis—which is both a pathological product and an aggravating factor throughout the entire course of IgAN, causing recurrent symptoms and protracted illness [16].

Professor Zhang Daning adheres to the four pathological bases of “deficiency, heat, dampness, and stasis.” Besides tonifying medicinals, he administers blood-activating agents — mild stasis requires activating blood and resolving stasis, while prolonged disease requires breaking stasis and promoting qi circulation. Professor Zhang prefers sweet-flavored medicinals for tonifying and harmonizing the middle, and most frequently uses medicinals targeting the liver-kidney and spleen-stomach meridians [17]. Professor Yang Nizhi established “supplementing qi and activating blood” as the general treatment principle, while also addressing qi circulation, diuresis, yin nourishment, blood enrichment, spleen-kidney warming and tonifying, and turbidity drainage and toxin descending [18].

3.1.3 Treatment Based on Damp-Heat Theory

Professor Zou Yanqin holds that IgAN is closely related to damp-heat, with wind-heat-dampness-stasis congealing in the kidney. The disease is located in the kidney but closely involves the lung and spleen. The pathogenesis of IgAN

relates to qi deficiency syndrome involving the five zang organs—depressed zang-fu function impairs qi and blood circulation, leading to stasis and toxin formation. External pathogens are invariably associated with wind, dampness, and heat; qi deficiency generates pathogens that manifest as damp-heat. The congelation of damp-heat and blood stasis is not only a critical pathogenic factor but also a primary driver of disease progression [19]. Professor Zou addresses this pathogenesis through treatment methods of clearing heat, draining dampness, dispelling wind, and unblocking collaterals, commonly using Abelmoschus manihot flower and Coix seed to clear heat and eliminate dampness, and insect medicinals to dispel wind and unblock collaterals [20].

3.1.4 Treatment Based on Triple Energizer Theory

As recorded in Lei Jing·Zang Xiang Lei (Classified Canon·Zang-Fu Manifestations): "When the upper energizer fails to regulate, water overflows the highlands; when the middle energizer fails to regulate, water remains in the middle; when the lower energizer fails to regulate, water disrupts urination and defecation." Renal edema is closely related to the triple energizer. Professor Chen Yiping, based on years of clinical experience, developed the "regulating the triple energizer with differentiated treatment" approach, with the key being to unblock stagnant qi and blood in the triple energizer, while also applying the "harmonizing the lesser yang" method to regulate systemic qi movement. The triple energizer serves as both the passage for qi movement and the site of qi transformation. In the early stage, upper energizer syndrome predominates when vital energy is sufficient and pathogens are superficial, allowing the use of heat-clearing, throat-soothing, and blood-cooling medicinals. In prolonged disease, the condition primarily involves the lower energizer with lower energizer deficiency, triple energizer qi stagnation, and concurrent deficiency and pathogen retention. Professor Chen advocates simultaneous attack and supplementation, emphasizing qi-regulating and qi-blood supplementing medicinals. Her self-formulated prescription uses Huangqi, Bupleurum, Chuanxiong, and Polygonatum as sovereign herbs, with modifications based on syndrome differentiation [21].

Professor Wang Yaoxian also considers triple energizer heat pathogen as the core TCM pathogenesis of IgAN. He proposes "heat binding in the triple energizer with renal collateral masses" as the central mechanism. Treatment is differentiated by the three energizers: upper energizer heat requires dispersing depressed heat, dispelling wind, cooling blood, and resolving masses; middle energizer heat requires clearing heat and resolving dampness; lower energizer heat requires draining turbid heat, resolving masses, and consolidating the root [22].

3.1.5 reatment Based on Kidney Deficiency

Whether in early or advanced IgAN, the pathogenesis involves mixed deficiency and excess, with kidney deficiency consistently participating. National Master of TCM Zhang Qi considers liver-kidney yin deficiency or qi-yin deficiency as internal factors underlying IgAN hematuria. Kidney deficiency is the pathogenic foundation, and subsequent symptoms such as "low back pain," "edema," and "consumptive disease" further damage kidney yin and yang. Professor Zhang emphasizes that "blood is the source that nourishes life" and that persistent hematuria or proteinuria impairs the body's resistance to pathogens. Deficiency is only the internal factor; damp-heat toxins and blood stasis are also causative. Treatment should address the root by tonifying the kidney [23].

3.2 Western Medicine

3.2.1 Treatment Principles

In September 2025, KDIGO formally released the KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV). This represents the first standalone guideline specifically addressing IgAN, marking a significant milestone as IgAN is no longer subsumed under the general glomerular diseases guideline. The guideline was co-chaired by Professor Jürgen Floege from Germany and Professor Brad Rovin from the United States, and published in Kidney International in September 2025.

The 2025 KDIGO guideline achieves a paradigm shift in treatment philosophy. Compared to the previous version, it encourages more aggressive renal biopsy policies and recommends more stringent proteinuria targets. For the first time, the guideline proposes "simultaneous initiation" of interventions targeting two major pathological processes: (1) etiological intervention—using therapies that prevent or reduce pathogenic IgA production and IgA/IgA and IgA/IgG immune complex formation (currently limited to targeted-release budesonide (Nefecon), reduced-dose systemic glucocorticoids, and, in Chinese patients, mycophenolate mofetil); and (2) management of consequences—addressing the consequences of nephron loss from existing IgAN, including healthy lifestyle education, RAS blockers, SGLT2 inhibitors, and/or dual endothelin angiotensin receptor antagonists.

For patients at risk of progressive kidney function loss, the treatment goal is to reduce the rate of kidney function decline to physiological levels (<1 ml/min/year for most adults). Proteinuria targets are also stricter, recommending <0.5 g/day, with <0.3 g/day being ideal. The guideline emphasizes individualized treatment and stratified management [25][42].

3.2.2 Supportive Therapy

RAS Blockers: Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) remain first-line agents for IgAN, offering both antihypertensive effects and proteinuria reduction while slowing renal damage. The 2025 KDIGO guideline maintains RAS blockers as foundational therapy. Although a meta-analysis suggested that combination therapy may reduce proteinuria more effectively than monotherapy [24], the 2025 KDIGO guideline continues the recommendation against combination use [25].

SGLT2 Inhibitors: Dapagliflozin and other SGLT2 inhibitors have demonstrated renal protective effects in the DAPA-CKD

trial, becoming important supportive therapies for IgAN. The 2025 KDIGO guideline has incorporated SGLT2 inhibitors into foundational therapy recommendations, alongside RAS blockers as first-line supportive agents.

3.2.3 Immunosuppressive Therapy

Glucocorticoids: These agents possess non-specific immunosuppressive and anti-inflammatory properties. In the 2025 KDIGO guideline, reduced-dose systemic glucocorticoids remain an option for reducing pathogenic IgA production. During administration, gastric and bone protection should be considered to avoid peptic ulcers, perforation, and osteoporosis.

Mycophenolate Mofetil (MMF): The 2025 KDIGO guideline specifically notes that in Chinese IgAN patients, MMF can serve as a therapeutic option for reducing pathogenic IgA production. A study by Liu et al. demonstrated that while the glucocorticoid plus MMF group showed no significant difference in proteinuria reduction compared to glucocorticoid monotherapy, the combination group had significantly fewer side effects [26].

Hydroxychloroquine (HCQ): A study from Peking University First Hospital showed that HCQ was slightly less effective than glucocorticoids in reducing proteinuria but had significantly fewer adverse events [27]. No guideline currently recommends HCQ for IgAN.

3.2.4 Novel Targeted Therapies

1) Complement Pathway Inhibitors

Iptacopan (Fabhalta®): An oral, first-in-class, targeted B-factor inhibitor that selectively inhibits the alternative complement pathway. The Phase 3 APPLAUSE-IgAN trial (NCT04578834)—a randomized, double-blind, placebo-controlled study—enrolled adult IgAN patients with 24-hour UPCR ≥1 g/g. The 9-month interim analysis showed that iptacopan reduced 24-hour UPCR by 38.3% from baseline, significantly superior to placebo (P<0.0001). In the East Asian patient subgroup, iptacopan similarly demonstrated clinically meaningful proteinuria reduction (−38.0%) with favorable safety. Iptacopan also selectively inhibited the alternative complement pathway, with significant reductions in serum Wieslab activity, plasma Bb, and sC5b-9, and a 97.6% median reduction in urinary sC5b-9. Based on these results, APPLAUSE-IgAN became the first Phase 3 trial demonstrating clinical benefit of alternative complement pathway inhibition in IgAN. The US FDA granted accelerated approval for iptacopan based on these findings. In October 2025, Novartis announced positive topline results from the APPLAUSE-IgAN trial, with iptacopan meeting the primary endpoint of eGFR slope reduction [29][30][43].

Narsoplimab (OMS721): A MASP-2-targeting monoclonal antibody designed to block the lectin complement pathway. However, the Phase 3 ARTEMIS-IgAN trial was terminated in 2025 after failing to meet the primary endpoint of statistically significant proteinuria reduction, and development for IgAN has been discontinued [35][36].

Cemdisiran (ALN-CC5): An RNA interference therapeutic targeting C5. A Phase 2, 36-week, double-blind, randomized controlled trial randomized patients with 24-hour proteinuria ≥1 g in a 2:1 ratio to cemdisiran 600 mg subcutaneously or placebo every 4 weeks. Results demonstrated potential for proteinuria reduction with favorable tolerability [37].

2) Endothelin Receptor Antagonists

Sparsentan: A novel, non-immunosuppressive, single-molecule dual endothelin angiotensin receptor antagonist (DEARA). The Phase 3 PROTECT study (NCT03762850) was a randomized, double-blind, active-controlled, multicenter trial enrolling 404 high-risk IgAN patients (proteinuria ≥1.0 g/day), comparing sparsentan (n=202) to maximally tolerated irbesartan (n=202) over 110 weeks. Two-year results demonstrated that sparsentan was significantly superior to maximally tolerated irbesartan in proteinuria reduction, with comparable safety. Post-hoc analyses showed significantly fewer patients progressing to CKD stages 4 or 5 in the sparsentan group, and significantly longer time to reach CKD stages 4 or 5. In proteinuria complete remission analysis (<0.3 g/day), 21% of patients achieved complete remission; these patients showed smaller eGFR decline (−4.0 vs −8.6 ml/min/1.73m²) and slower eGFR decline rates (−0.7 vs −4.2 ml/min/1.73m²/year) [31][32][44]. The 2025 KDIGO guideline has incorporated sparsentan into treatment recommendations.

Atrasentan (Vanrafia®): A potent, highly selective ETA receptor antagonist. The Phase 3 ALIGN study (NCT04573478) is an ongoing randomized, double-blind, placebo-controlled trial enrolling adult IgAN patients with 24-hour total proteinuria ≥1 g/day on optimized supportive care. On April 3, 2025, the US FDA granted accelerated approval to atrasentan for proteinuria reduction in adults with primary IgAN at risk of rapid disease progression, based on the 36-week pre-specified interim proteinuria reduction data from ALIGN. Patients received atrasentan on top of RAS inhibitor-based supportive care (with or without SGLT2 inhibitors). Data demonstrated a 36.1% significant reduction in proteinuria compared to placebo (P<0.0001), with efficacy observed as early as week 6 and sustained through week 36 [39][45]. Continued approval is contingent upon verification of clinical benefit in the ongoing ALIGN study at week 136, with eGFR data expected in 2026.

3) Mucosal Immunity-Targeted Agents

Targeted-Release Budesonide (Nefecon®): Approved by the FDA in late 2021, this formulation delivers the drug precisely to the ileocecal region of the intestine, blocking pathogenic IgA production. The 2025 KDIGO guideline lists it as the only agent currently proven to significantly reduce pathogenic IgA production and immune complexes. The multicenter NefIgArd trial, published in Kidney International, demonstrated reduced UPCR and slower eGFR decline [33][34].

4) BAFF/APRIL Axis-Targeted Therapies

Telitacicept: A dual inhibitor targeting both BLyS and APRIL. A Phase 3, multicenter, randomized, double-blind, placebo-controlled trial enrolling 318 high-risk IgAN patients

(24-hour UPCR ≥0.8 g/g or total proteinuria ≥1.0 g/day) showed that telitacicept reduced 24-hour UPCR by 55% compared to placebo at 39 weeks (P<0.0001), with favorable safety. Results were presented at ASN Kidney Week 2025.
*Povetacicept: A dual BAFF and APRIL inhibitor. The ongoing RUBY-3 Phase 1/2 open-label study showed 64% proteinuria reduction from baseline at 48 weeks, with significant Gd-IgA1 reduction and stable eGFR. Based on these positive results, povetacicept has received FDA Breakthrough Therapy Designation, with the Phase 3 RAINIER study underway.

*Zigakibart (BION-1301): An APRIL-targeting humanized monoclonal antibody. Phase 1/2 studies showed 60% proteinuria reduction, stable renal function, and sustained reductions in IgA and related biomarkers. Based on these results, zigakibart has entered the Phase 3 BEYOND study (randomized, double-blind, placebo-controlled), which Novartis announced the initiation of on August 15, 2025 [38].

*Sibeprenlimab: An APRIL-targeting monoclonal antibody. Based on positive results from the Phase 2 ENVISION trial, the FDA granted Breakthrough Therapy Designation. In March 2025, the company announced submission of a Biologics License Application (BLA), supported by Phase 2 ENVISION and Phase 3 VISIONARY trial results. In November 2025, the FDA granted accelerated approval for this indication.

*Atacicept: A BLyS and APRIL-targeting fusion protein. The Phase 2b ORIGIN study met its primary endpoint at 24 weeks (significant UPCR reduction), with efficacy sustained through 36 weeks and stable eGFR. Open-label extension follow-up to 96 weeks showed continued improvement in key IgAN parameters.

4. Summary and Outlook

The pathogenesis of IgAN remains incompletely elucidated, and clinical treatment still faces challenges. The release of the 2025 KDIGO guideline marks a paradigm shift—from "sequential treatment" to "simultaneous initiation" of etiological intervention and complication management, with stricter treatment targets (eGFR decline <1 ml/min/year, proteinuria <0.5 g/day), providing clearer pathways for clinical practice.

Traditional Chinese medicine, with its holistic approach and zang-fu yin-yang syndrome differentiation, has developed multiple treatment systems addressing wind pathogen, kidney deficiency with blood stasis, damp-heat, and triple energizer, demonstrating unique advantages in symptom improvement and delaying disease progression. Western medicine, centered on targeted therapy, continues to advance with both conventional agents (RAS blockers, SGLT2 inhibitors) and novel therapeutics (complement inhibitors, endothelin receptor antagonists, BAFF/APRIL-targeted agents) in parallel, with multiple agents having received FDA approval or entered Phase 3 trials, offering new hope for patients.

The integration of TCM and Western medicine can leverage the strengths of both approaches—TCM for holistic regulation and complication reduction, Western medicine for precise targeted intervention—representing a promising direction for IgAN management. Future research should further elucidate pathogenic mechanisms, refine individualized treatment protocols, and expand clinical practice and evidence accumulation for integrated approaches, ultimately providing more effective and safer treatment strategies for IgAN patients.

References

[1] A. McGrogan, C.F.M. Franssen, and C.S. de Vries, "The incidence of primary glomerulonephritis worldwide: a systematic review of the literature," Nephrol Dial Transplant, vol. 26, no. 2, pp. 414-430, 2011.
[2] X.W. Du, D.M. Xiao, C.Q. Ao, et al., "Disease burden of IgA nephropathy in Chinese adults," China Journal of Pharmaceutical Economics, vol. 17, no. 7, pp. 46-52, 2022.
[3] L. Zhang, M.H. Zhao, L. Zuo, et al., "China Kidney Disease Network (CK-NET) 2016 Annual Data Report," Kidney Int Suppl (2011), vol. 10, no. 2, pp. e97-e185, 2020.
[4] H. Suzuki, R. Fan, Z.X. Zhang, et al., "Aberrantly glycosylated IgA1 in IgA nephropathy patients is recognized by IgG antibodies with restricted heterogeneity," J Clin Invest, vol. 119, no. 6, pp. 1668-1677, 2009.
[5] A.G. Gharavi, Z. Moldoveanu, R.J. Wyatt, et al., "Aberrant IgA1 glycosylation is inherited in familial and sporadic IgA nephropathy," J Am Soc Nephrol, vol. 19, pp. 1008-1014, 2008.
[6] Y. Tang, Y. Zhu, H. He, et al., "Gut Dysbiosis and Intestinal Barrier Dysfunction Promotes IgA Nephropathy by Increasing the Production of Gd-IgA1," Front Med (Lausanne), vol. 9, p. 944027, 2022.
[7] J. Li, J. Gao, and R.H. Lv, "Pathogenesis of primary glomerular diseases treated from wind pathogen," China Journal of Basic Medicine in Traditional Chinese Medicine, vol. 11, no. 10, pp. 731-733, 2005.
[8] J. Li, H.T. Xing, Y.T. Dou, et al., "Professor Huang Wenzheng's understanding and medication experience of 'internal wind' in kidney wind disease," Guangming Journal of Chinese Medicine, vol. 31, no. 1, pp. 34-36, 2016.
[9] S.J. Ma and Y. Zhang, "Zhang Yu's approach to treating proteinuria in IgA nephropathy from wind pathogen," Journal of Traditional Chinese Medicine, vol. 37, no. 2, pp. 341-344, 2022.
[10] L. Zhang, "Cao Shili's experience in treating IgA nephropathy from wind pathogen," Liaoning Journal of Traditional Chinese Medicine, vol. 44, no. 7, pp. 1375-1376, 2017.
[11] L.S. Li, M.M. Zhao, and Y. Zhang, "Zhang Yu's experience in diagnosing and treating IgA nephropathy based on the complex pathogenesis network of 'deficiency-wind-stasis-toxin'," World Journal of Integrated Traditional and Western Medicine, vol. 12, no. 4, pp. 450-455+472, 2017.
[12] Y. Si, L.M. Zhang, and Y. Zhang, "Data mining study on Professor Zhang Yu's medication patterns in treating IgA nephropathy," in Proceedings of the 2018 Annual Academic Conference of the Nephrology Professional

Committee of the Chinese Association of Integrative Medicine, Beijing, 2018, p. 429.
[13] S.N. Dong, Y.G. Wang, and W.Z. Huang, "Preliminary exploration of Huang Wenzheng's experience in applying Chan Can Shen Feng Tang," Liaoning Journal of Traditional Chinese Medicine, vol. 38, no. 9, pp. 1735-1736, 2011.
[14] M.Z. Zhang, D.N. Zhang, M.Y. Zhang, et al., "Clinical study on treating 160 cases of IgA nephropathy with kidney-tonifying and blood-activating method," Journal of Traditional Chinese Medicine, no. 1, pp. 38-40, 2006.
[15] J.Y. Gao, M.Z. Zhang, and D.N. Zhang, "Therapeutic observation on kidney-tonifying and blood-activating method for chronic glomerulonephritis," Tianjin Journal of Traditional Chinese Medicine, vol. 31, no. 3, pp. 145-147, 2014.
[16] Y.M. Luo, X.P. Li, T.X. Hu, et al., "Yang Nizhi's experience in applying qi-supplementing and blood-activating method for IgA nephropathy," Liaoning Journal of Traditional Chinese Medicine, vol. 46, no. 8, pp. 1605-1607, 2019.
[17] Z. Shi, "Meta-analysis of kidney-tonifying and blood-activating method for IgA nephropathy and study on Professor Zhang Daning's medication patterns for IgA nephropathy" [Master's thesis], Tianjin University of Traditional Chinese Medicine, 2020.
[18] W.F. Wang, "Study on Professor Yang Nizhi's academic thought and clinical experience in treating chronic kidney disease" [Master's thesis], Guangzhou University of Chinese Medicine, 2015.
[19] W. Sun, A.P. Zeng, G. Wang, et al., "Exploration of the TCM pathogenesis of IgA nephropathy," Modern Journal of Integrated Traditional Chinese and Western Medicine, vol. 8, no. 4, pp. 522-523, 1999.
[20] K. Gao, P. Xia, Y. Lu, et al., "Analysis of National Master of TCM Professor Zou Yanqin's academic characteristics and medication patterns in treating IgA nephropathy based on data mining," Modern Chinese Clinical Medicine, vol. 27, no. 6, pp. 27-32, 2020.
[21] Q. Zhang, Y.P. Chen, X.W. Zhang, et al., "Professor Chen Yiping's experience in treating IgA nephropathy with the 'regulating the triple energizer' method," China Medical Herald, vol. 19, no. 23, pp. 142-145+161, 2022.
[22] Y.X. Liu, Y.X. Wang, H.F. Liu, et al., "Application of heat-clearing and mass-resolving method in differentiating and treating IgA nephropathy based on triple energizer theory," Global Traditional Chinese Medicine, vol. 15, no. 5, pp. 854-857, 2022.
[23] J.Z. Wang, Y.B. Huang, and Q. Zhang, "Re-analysis of Professor Zhang Qi's experience in treating hematuria in IgA nephropathy," Heilongjiang Traditional Chinese Medicine, no. 2, pp. 4-5, 2005.
[24] M. Zhao, R. Wang, Y. Yu, et al., "Efficacy and Safety of Angiotensin-Converting Enzyme Inhibitor in Combination with Angiotensin-Receptor Blocker in Chronic Kidney Disease Based on Dose: A Systematic Review and Meta-Analysis," Front Pharmacol, vol. 12, p. 638611, 2021.
[25] KDIGO, "KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV)," Kidney Int, 2025.
[26] J.H. Hou, W.B. Le, N. Chen, et al., "Mycophenolate Mofetil Combined with Prednisone Versus Full-Dose Prednisone in IgA Nephropathy with Active Proliferative Lesions: A Randomized Controlled Trial," Am J Kidney Dis, vol. 69, no. 6, pp. 788-795, 2017.
[27] Y.Z. Yang, P. Chen, L.J. Liu, et al., "Comparison of the effects of hydroxychloroquine and corticosteroid treatment on proteinuria in IgA nephropathy: a case-control study," BMC Nephrol, vol. 20, no. 1, p. 297, 2019.
[28] M.L. Zoler, "New DAPA-CKD Analysis Hints at Dapagliflozin for IgA Nephropathy" [Internet], Medscape, Apr. 20, 2021. Available: https://www.medscape.com/viewarticle/949863
[29] H. Wang, X. Feng, B. Song, and F. Xie, "Iptacopan: a targeted B-factor inhibitor of the complement system," Journal of Clinical Pharmacotherapy, vol. 19, no. 10, pp. 22-27, 2021.
[30] J. Barratt, B. Rovin, H. Zhang, et al., "Interim analysis of a Phase 2 dose ranging study to investigate the efficacy and safety of iptacopan in primary IgA nephropathy" [Abstract], presented at ERA-EDTA Congress, Berlin, Germany, Jun. 5-8, 2021.
[31] Travere Therapeutics, Inc., "Travere Therapeutics Announces Successful Outcome from Type A Meeting with U.S. FDA for Sparsentan in Focal Segmental Glomerulosclerosis" [Internet], 2022. Available: https://ir.travere.com/news-releases/news-release-details/travere-therapeutics-announces-successful-outcome-type-meeting
[32] R. Komers, U. Diva, J.K. Inrig, et al., "Study Design of the Phase 3 Sparsentan Versus Irbesartan (DUPLEX) Study in Patients with Focal Segmental Glomerulosclerosis," Kidney Int Rep, vol. 5, no. 4, pp. 494-502, 2020.
[33] J. Barratt, R. Lafayette, J. Kristensen, et al., "Results from part A of the multi-center, double-blind, randomized, placebo-controlled NefIgArd trial, which evaluated targeted-release formulation of budesonide for the treatment of primary immunoglobulin A nephropathy," Kidney Int, vol. 103, no. 2, pp. 391-402, 2023.
[34] G. Ismail, B. Obrişcă, R. Jurubiţă, et al., "Budesonide versus systemic corticosteroids in IgA Nephropathy: A retrospective, propensity-matched comparison," Medicine (Baltimore), vol. 99, no. 26, p. e21000, 2020.
[35] National Medical Products Administration Center for Drug Evaluation, "Clinical trial implied approval" [EB/OL], 2022. Available: https://www.cde.org.cn/main/xxgk/listpage/4b5255eb0a84820cef4ca3e8b6bbe20c
[36] R.A. Lafayette, B.H. Rovin, H.N. Reich, et al., "Safety, Tolerability and Efficacy of Narsoplimab, a Novel MASP-2 Inhibitor for the Treatment of IgA Nephropathy," Kidney Int Rep, vol. 5, no. 11, pp. 2032-2041, 2020.
[37] J. Barratt, S.C. Yeo, A. Fernström, et al., "Results from the Phase 2 Study of Cemdisiran in Adult Patients with IgA Nephropathy," Alnylam, Aug. 29, 2022.
[38] J. Barratt, "Updated Interim Results of a Phase 1/2 Study of BION-1301 in Patients with IgA Nephropathy" [Abstract], J Am Soc Nephrol, vol. 33, p. 503, 2022.

[39] N.E. Olson, “A Multi-Omics Approach to IgA Nephropathy Characterization in the NURTuRE Cohort Enables Precision-Based Treatment Approaches” [Abstract], J Am Soc Nephrol, vol. 33, p. 34, 2022.
[40] M. Takahara, T. Nagato, Y. Nozaki, et al., “A proliferation-inducing ligand (APRIL) induced hyper-production of IgA from tonsillar mononuclear cells in patients with IgA nephropathy,” Cell Immunol, vol. 341, p. 103925, 2019.
[41] J.R. Myette, T. Kano, H. Suzuki, et al., “A Proliferation Inducing Ligand (APRIL) targeted antibody is a safe and effective treatment of murine IgA nephropathy,” Kidney Int, vol. 96, no. 1, pp. 104-116, 2019.
[42] KDIGO, “KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV),” Kidney Int, 2025.
[43] J. Barratt, B. Rovin, H. Zhang, et al., “Iptacopan in Patients with IgA Nephropathy from East Asia: Interim Analysis of the Phase 3 APPLAUSE-IgAN Study,” Kidney Int Rep, 2025.
[44] H.J.L. Heerspink, B.H. Rovin, R. Komers, et al., “Association between Complete Proteinuria Remission and Kidney Function in the Phase 3 PROTECT Trial of Sparsentan in IgA Nephropathy,” Clin J Am Soc Nephrol, 2025.
[45] Novartis, “FDA Grants Accelerated Approval for Vanrafia® (atrasentan) for Proteinuria Reduction in Primary IgA Nephropathy” [Internet], Press Release, Apr. 3, 2025. Available: https://www.novartis.com/news/media-releases
[46] Novartis, “Novartis announces positive top-line results from Phase III APPLAUSE-IgAN study of Fabhalta® (iptacopan) in IgA nephropathy (IgAN)” [Internet], Press Release, Oct. 2025. Available: https://www.novartis.com/news/media-releases