ARTYKUŁ ORYGINALNY / ORIGINAL PAPER
Otrzymano/Submitted: 16.12.2024 • Zaakceptowano/Accepted: 30.04.2025

Therapeutic monoclonal antibodies: new opportunities in nephrology

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Abstract

Introduction. Monoclonal antibodies (mAbs) are increasingly utilized in clinical practice due to their targeted mechanisms of action and favorable safety profiles. Their role in nephrology is expanding, offering novel treatment strategies for previously refractory renal diseases. ***Materials and methods.*** A systematic review of PubMed and Google Scholar was conducted, focusing on mAbs used in nephrology over the past two years. Inclusion criteria encompassed English-language studies with detailed mechanisms and clinical outcomes. ***Results.*** Twenty-seven studies were analyzed. Multiple mAbs have shown therapeutic benefits in renal diseases: sibeprenlimab, obinutuzumab, rituximab, belimumab, secukinumab, eculizumab, tocilizumab, daratumumab, isatuximab, adalimumab, fresolimumab, daclizumab, and abatacept. These agents demonstrated efficacy in conditions such as IgA nephropathy, lupus nephritis, membranous nephropathy, atypical hemolytic uremic syndrome, and minimal change disease, with positive outcomes in proteinuria reduction, renal function preservation, and steroid-sparing effects. ***Conclusion.*** mAbs offer a targeted, safer alternative to traditional immunosuppressants, potentially improving long-term renal outcomes. However, further studies are required to determine their long-term impact on survival and disease remission. *(Farm Współ 2025; 18: 157-169) doi: 10.53139/FW.20251815*

Keywords: monoclonal antibodies, nephrology, IgA nephropathy, lupus nephritis, glomerular disease

Introduction

Monoclonal antibodies (mAbs) have become the main biopharmaceuticals and have dominated the market due to their efficacy and broad applications [1]. The breakthrough development of antibody phage display technology by John McCafferty and Sir Gregory Winter in the early 1990s facilitated the discovery and production of human antibodies and paved the way for advanced therapeutics. Since the 1980s, advancements in recombinant DNA technology have expanded mAbs' use across a spectrum of diseases, including cancer, asthma, and cardiovascular diseases. Monoclonal antibodies have significantly transformed treatment paradigms across various diseases [1,2].

These biologic agents, designed to target specific antigens, have shown remarkable efficacy in conditions ranging from autoimmune disorders to cancer to infectious diseases. In oncology, the introduction of mAbs (pembrolizumab and nivolumab) has redefined therapeutic strategies, which resulted in improved survival rates in melanoma and non-small cell lung cancer [3]. Similarly, in the context of COVID-19, monoclonal antibodies bamlanivimab and casirivimab-imdevimab have provided critical options for preventing severe outcomes in high-risk patients [4]. The precision and adaptability of mAbs have made them indispensable tools in modern medicine, offering tailored treatment approaches with the potential for fewer adverse effects than traditional therapies.

In recent years, the development of mAbs has also significantly advanced nephrology, offering new therapeutic avenues for previously challenging renal diseases [5-7]. These biologics, designed to target specific immune pathways and cellular mechanisms, have shown remarkable efficacy in IgA nephropathy, lupus nephritis, and glomerular diseases presenting with nephrotic syndrome. Notable examples include sibeprenlimab, which

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targets the APRIL pathway in IgA nephropathy [5], and obinutuzumab, a next-generation anti-CD20 antibody that has shown promise in reducing proteinuria in treatment-resistant glomerular diseases presenting with nephrotic-range proteinuria [6, 7]. These advancements represent a significant leap forward, underscoring the potential of monoclonal antibodies to transform nephrology by addressing unmet clinical needs and improving patient outcomes [5-7].

Materials and methods

A systematic literature review was conducted using electronic databases (PubMed) and academic search engines (Google Scholar). The search strategy employed combinations of keywords such as "monoclonal antibodies", "nephrology", "IgA nephropathy," "lupus nephritis", "nephrotic syndrome", and "autoimmune kidney diseases". Studies were included if they detailed monoclonal antibodies' development, application, or clinical outcomes in nephrology, specifically focusing

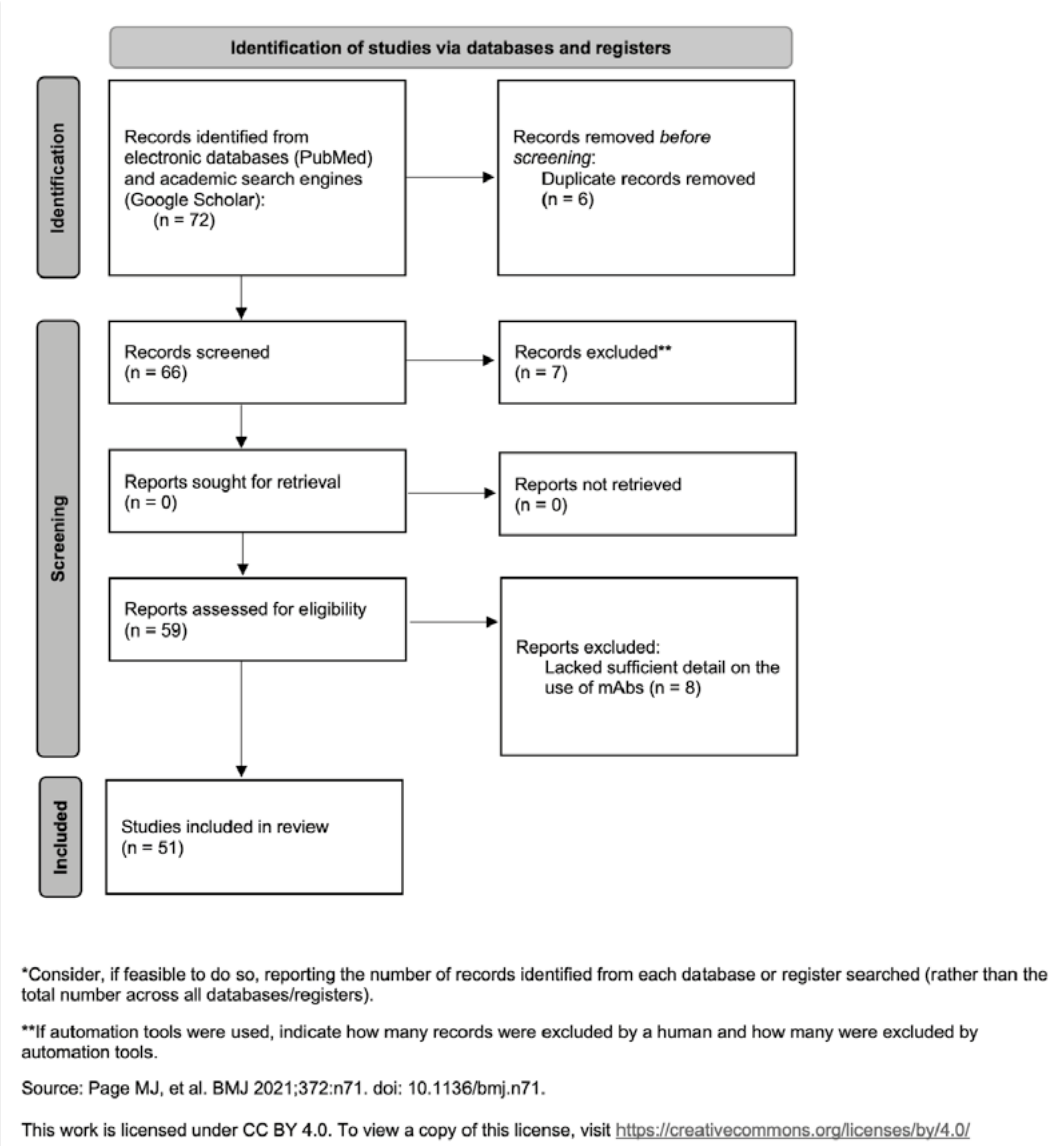

Figure 1. The process of selecting articles for review according to PRISMA

on those introduced within the last two years. Only articles in English were reviewed. Studies that focused on non-renal conditions, lacked detailed descriptions of the monoclonal antibody mechanisms, or did not present clinical outcomes relevant to nephrology were excluded.

Fifty-one research papers meeting the inclusion criteria were selected for analysis. Data extracted from each study included the type of monoclonal antibodies used, mechanisms of action, treatment regimens, patient populations, clinical outcomes, and reported adverse effects. The extracted data were organized into tables to provide a comprehensive overview of the efficacy and safety profiles of these monoclonal antibodies in nephrology. This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure rigorous and transparent reporting of the findings. Particular attention was paid to evaluating the included studies' methodological quality to assess the reliability of their conclusions. Any potential biases or inconsistencies in the data were identified by the authors and discussed to provide a balanced interpretation of the results. By conducting this review, the authors aim to inform future research and guide clinical practice regarding the use of monoclonal antibodies in the treatment of renal diseases.

Recent advances in monoclonal antibody use in nephrology

Over the past few years, nephrology has witnessed significant breakthroughs by introducing several novel monoclonal antibodies. These therapies offer promising alternatives to existing treatments, providing enhanced efficacy and improved patient outcomes. Below are three of the most impactful monoclonal antibodies recently introduced in nephrology:

Sibeprenlimab

Sibeprenlimab is a humanized IgG2 monoclonal antibody targeting a Proliferation-Inducing Ligand (APRIL – CD256 – member of the TNF superfamily), a critical mediator in the pathogenesis of IgA nephropathy (IgAN).

IgA nephropathy is the most common primary glomerulonephritis worldwide, characterized by the deposition of IgA-containing immune complexes in the glomerular mesangium, leading to progressive renal dysfunction in many patients. Current standard treatment for IgAN primarily includes renin-angiotensin system (RAS) inhibitors to control proteinuria and hypertension and corticosteroids and immunosuppressive agents for patients with a more aggressive disease course. However, these therapies often carry significant side effects such as increased risk of infections, hyperglycemia, hypertension, osteoporosis, and gastrointestinal disturbances, as well as potential long-term organ damage [8-10].

Neutralizing APRIL sibeprenlimab offers a targeted approach, reducing the survival and differentiation of plasma cells responsible for aberrant glycosylation of IgA. This mechanism directly addresses the pathogenic process in IgAN, unlike broader immunosuppressants. Mathur et al. performed a study that underscored the efficacy of sibeprenlimab, demonstrating a significant, dose-dependent reduction in proteinuria over 12 months. Specifically, reductions in the 24-hour urinary protein-to-creatinine ratio ranged from 47.2% at a 2 mg/kg dose to 62.0% at an 8 mg/kg dose, compared to a 20.0% reduction in the placebo group in this study. Furthermore, sibeprenlimab stabilized eGFR, with the 4 mg/kg dose group showing an improvement of +7.6 ml/min/1.73 m^2 over placebo, indicating its potential to preserve renal function. Compared to traditional immunosuppressants, sibeprenlimab exhibits a more favorable safety profile, with adverse event rates comparable to placebo and fewer systemic adverse effects [5, 11].

The use of sibeprenlimab can slow disease progression and preserve renal function over the long term, potentially delaying or preventing the onset of end-stage renal disease (ESRD). The observed stability in eGFR across treatment groups in the trial suggests that sibeprenlimab may effectively attenuate the decline in renal function that typically characterizes IgAN progression. Ongoing longitudinal studies aim to assess its efficacy in reducing the need for dialysis or transplantation and improving overall quality of life for patients with IgAN. This long-term efficacy, combined with its targeted mechanism of action and safety profile, positions sibeprenlimab as a promising therapeutic option in managing IgAN [5,11].

Obinutuzumab

Nephrotic syndrome is characterized by severe proteinuria, hypoalbuminemia, and edema, typically managed with corticosteroids and immunosuppressive agents, such as cyclophosphamide or rituximab. Despite these interventions, many patients encounter relapses and significant side effects from prolonged immunosuppression [12]. Obinutuzumab provides a revolutionary alternative, potentially reducing proteinuria more effec-

tively and improving long-term outcomes in patients resistant to traditional therapies.

As a type II IgGa subclass anti-CD20 monoclonal antibody, it offers superior B-cell depletion compared to first-generation antibodies, including rituximab. Its enhanced efficacy is attributed to more potent antibody-dependent cellular cytotoxicity (ADCC) and direct cell death induction. In clinical studies, obinutuzumab has demonstrated notable effectiveness in treating glomerular diseases that can manifest as steroid-resistant nephrotic syndrome, particularly membranous nephropathy (MN) and lupus nephritis.

In a study of 14 patients with multidrug-dependent nephrotic syndrome, 9 achieved stable complete remission after 20 months of follow-up. Compared to rituximab, obinutuzumab has shown improved progression-free survival, though it has been associated with an increased incidence of serious adverse effects (OR 1.29, 95% CI 1.13–1.48, P < 0.001) [12-18].

The prolonged B-cell depletion offered by obinutuzumab may translate into extended remission periods and a reduced need for additional corticosteroids and immunosuppressants. In a study by Sethi on 10 patients with refractory MN treated with obinutuzumab, 40% achieved complete remission and 50% achieved partial remission within 6 months. These outcomes were maintained in those followed for up to 24 months [12]. In a study by Yuxin Lin of 18 patients with refractory MN treated with obinutuzumab, partial remission (PR) was achieved in 66.7% and complete remission (CR) in 27.8%, with 6-month and 12-month remission rates of 72.2% and 88.9%, respectively. The median time to achieve any form of remission after the first dose of obinutuzumab was 2.7 months, while those attaining CR reached this status in a median of 9.4 months. Over a median follow-up period of 13.6 months, the median first relapse-free survival time was 9.8 months [7].

The long-term safety profile of obinutuzumab appears favorable, although some patients experienced mild infusion-related reactions and transient leukopenia. Future research will be crucial in confirming its impact on altering disease progression and improving renal survival rates [13-18].

Secukinumab

Secukinumab is a fully human monoclonal antibody that targets interleukin-17A (IL-17A), a cytokine involved in pro-inflammatory responses. It is currently used to treat various autoimmune diseases and is being investigated as a novel therapeutic option for lupus nephritis (LN), a severe complication of systemic lupus erythematosus (SLE).

Lupus nephritis is a severe manifestation of SLE that leads to kidney inflammation, significant morbidity, and can progress to end-stage renal disease (ESRD) if not properly managed. The standard treatment for LN typically involves high-dose corticosteroids combined with immunosuppressive drugs such as mycophenolate mofetil or cyclophosphamide. While these treatments are often effective in controlling the disease, they come with a high risk of adverse side effects, including infections, hypertension, and long-term organ damage. Moreover, some patients, particularly those with refractory or severe disease, do not achieve remission with these standard therapies.

Secukinumab, by targeting IL-17A (plays a critical role in promoting inflammation and tissue damage in autoimmune diseases, including lupus nephritis. This cytokine drives the recruitment of inflammatory cells into tissues, leading to renal inflammation and fibrosis, both of which contribute to kidney damage in LN. It provides more specific immune modulation, aiming to reduce renal inflammation and subsequent fibrosis in LN without broadly suppressing the entire immune system. This specificity could potentially reduce the overall burden of side effects associated with traditional immunosuppressive therapies. We identified three case-studies.

In a case study by Y. Satoh, a 62-year-old woman with a history of psoriasis vulgaris and systemic lupus erythematosus (SLE)-related lupus nephritis (LN) was treated with secukinumab after years of conventional therapies [19]. Secukinumab was introduced at a dose of 300 mg/week. Following its administration, a significant decrease in disease activity markers was observed. Notably, the patient's anti-dsDNA antibody level dropped from 46.6 to 3.2, serum creatinine and urine protein levels improved, and hypocomplementemia was resolved by the end of 30 days since secukinumab introduction. Both the SLE Disease Activity Index (SLEDAI) score and British Isles Lupus Assessment Group (BILAG) score improved, from 16 to 4 and 15 to 10, respectively [19].

In a case study by Masahiko Ochi, a 60-year-old male patient with secondary failure of adalimumab therapy for psoriasis, nephritis with severe kidney dysfunction was observed, necessitating hospitalization. On admission, the patient exhibited nephrotic syndrome, proteinuria, hematuria, and impaired kidney func-

tion (eGFR of 49.8 mL/min/1.73 m²). Despite previous treatments, including steroids, ultraviolet therapy, and etretinate, the nephritis persisted, and psoriasis relapsed with a high PASI score of 40. Secukinumab was introduced to maintain remission of psoriasis and nephritis. The patient improved significantly in both conditions, with remission of psoriasis and gradual improvement in nephritis. The treatment dosage of secukinumab was adjusted from weekly injections to once every 4 weeks after the induction phase [20].

In a study by Zhiqiang Cao, a 21-year-old female with persistent proteinuria and hyperuricemia was admitted to the nephrology department to evaluate and treat suspected focal segmental glomerulosclerosis (FSGS). In March 2021, the patient was hospitalized for severe psoriasis, and dermatologists recommended secukinumab. She received five subcutaneous injections of 300 mg over five weeks, followed by monthly maintenance injections. Within one week of initiating secukinumab, the patient's psoriatic lesions improved, with complete resolution by the first month, and her Psoriasis Area and Severity Index (PASI) dropped from 47 to 0. Remarkably, a sustained decrease in 24-hour urine protein and serum uric acid was observed along with psoriasis remission. By January 2022, her uric acid levels had normalized, and proteinuria had been significantly reduced. No adverse effects were noted from secukinumab therapy, and her weight decreased from 80 kg to 66 kg over two months, stabilizing at a BMI of 26.4 kg/m². Throughout this period, her serum creatinine remained within the normal range [21].

All three case studies demonstrate the potential of secukinumab to contribute to managing renal complications in patients with underlying nephrological diseases.

By effectively controlling renal inflammation and reducing reliance on corticosteroids, secukinumab can induce sustained renal remission and improve long-term outcomes for LN patients. Over time, this may contribute to better preservation of renal function, decreased progression to ESRD, and improved quality of life. However, long-term follow-up studies are essential to fully understand the drug's potential to prevent ESRD and improve patient survival rates.

Belimumab

This fully human monoclonal antibody inhibits B-lymphocyte stimulator (BLyS), a key factor in B-cell survival and autoantibody production. Initially approved for systemic lupus erythematosus (SLE), belimumab has since demonstrated efficacy in lupus nephritis (LN), a severe renal manifestation affecting up to 40% of SLE patients. The pivotal phase III BLISS-LN trial showed that adding belimumab to standard therapy significantly improved renal outcomes, including higher rates of complete renal response and reduced progression to kidney failure or flare-ups. Post hoc and open-label extension analyses further confirmed its role in preserving kidney function and maintaining proteinuria control [22]. A recent meta-analysis of randomized controlled trials reaffirmed belimumab's favorable impact on renal response and its safety profile in patients with LN, highlighting its value as an adjunct to standard immunosuppressive regimens [23-25]. These findings support belimumab's growing role as a targeted therapy for LN.

Tocilizumab

This humanized monoclonal antibody targeting the interleukin-6 receptor (IL-6R) was investigated for its immunomodulatory effects in autoimmune-related renal disorders. IL-6 plays a central role in B cell activation, antibody production, and T cell differentiation, making its blockade a rational strategy in conditions like antibody-mediated rejection (ABMR) after kidney transplantation and desensitization in highly sensitized transplant candidates. Studies show that tocilizumab can significantly reduce donor-specific anti-HLA antibodies, improve histologic lesions associated with ABMR, and stabilize kidney function in patients resistant to standard therapies [26,27]. Additionally, its use in COVID-19-infected kidney transplant recipients helped modulate the cytokine storm, although outcomes were variable depending on the severity of inflammation at baseline [28]. While tocilizumab does not always improve short-term transplant access, it may enhance long-term graft survival by inhibiting memory B-cell maturation and alloantibody rebound, underscoring its potential in personalized renal immunotherapy [27,29].

Fresolimumab

This humanized monoclonal antibody neutralizes all three isoforms of transforming growth factor-beta (TGF-β), a key cytokine implicated in the progression of renal fibrosis. It has been explored primarily in the treatment of focal segmental glomerulosclerosis (FSGS), where TGF-β overexpression contributes to podocyte injury and extracellular matrix accumulation. In a phase I trial, single-dose fresolimumab was well-tolerated in patients with treatment-resistant primary FSGS, with

some individuals, particularly Black patients, demonstrating reductions in proteinuria and stabilization of kidney function. However, subsequent phase II trials in FSGS showed only modest effects, and results were confounded by early trial termination and small sample sizes [30]. Despite limited clinical efficacy, fresolimumab proves that systemic TGF-β blockade may attenuate fibrotic progression. However, targeted delivery to fibrotic sites might be necessary to optimize efficacy while minimizing systemic effects [31].

Daclizumab

This humanized monoclonal antibody targeting the alpha subunit (CD25) of the interleukin-2 receptor (IL-2R) has been explored primarily in the context of kidney transplantation. It acts by inhibiting IL-2-mediated activation of T cells, reducing the risk of acute rejection. Clinical studies have demonstrated that daclizumab is effective as induction therapy in renal transplant recipients, particularly in those at low to moderate immunological risk. However, in high-risk patients, rabbit antithymocyte globulin (rATG) has shown superior long-term outcomes in reducing biopsy-proven acute rejection [32]. Moreover, daclizumab was found to alter the renal handling of soluble IL-2Rα (sIL-2Rα) by forming large immune complexes, thereby inhibiting its filtration and urinary excretion, which may provide a potential biomarker for drug monitoring [33]. Despite its immunosuppressive efficacy, daclizumab is no longer in clinical use due to safety concerns, but it played a significant role in shaping targeted immunomodulatory strategies in renal transplantation [34].

Abatacept

This CTLA-4 Ig fusion protein functions by modulating T-cell activation through the inhibition of the CD80/CD86–CD28 costimulatory pathway. It has emerged as a promising targeted therapy for immune-mediated renal diseases, particularly minimal change disease (MCD) associated with elevated urinary CD80 levels. In a compelling case report, abatacept effectively maintained long-term remission in a patient with steroid- and calcineurin-dependent MCD, significantly reducing the frequency and severity of relapses. This clinical benefit was sustained for over six years, with abatacept enabling the tapering of concurrent immunosuppressants and being well-tolerated. These findings support the potential of abatacept as a mechanistic-based approach in select patients with CD80-positive nephrotic syndrome [35].

Rituximab

This chimeric monoclonal antibody targeting CD20 has emerged as a potential treatment for steroid-resistant nephrotic syndrome (SRNS), particularly in pediatric populations. Its application in nephrology has shown promising results, especially in children who have not responded to corticosteroids and calcineurin inhibitors (CNIs), which are typically used as first-line therapies [36].

An extensive international study involving 246 children demonstrated varying remission rates with rituximab, dependent on prior treatment with CNIs. Among patients with CNI-resistant SRNS (defined as failure to achieve remission after at least 6 months of CNI therapy), 35% to 39% achieved partial or complete remission within 12 to 24 months following rituximab administration. In contrast, patients who received less than 6 months of CNI treatment before rituximab experienced significantly higher remission rates, ranging from 42% at 3 months to 60% at 24 months. The study concluded that rituximab is generally well-tolerated, with mild adverse events reported in approximately 30% of patients. However, its effectiveness in SRNS may depend on the timing of its administration and prior treatment history [36,37].

Further studies, including those conducted in adult populations with membranous nephropathy, have demonstrated rituximab's efficacy in achieving both partial and complete remission in 57% to 89% of cases. Compared to traditional treatments such as cyclophosphamide, rituximab offers a favorable safety profile, with a lower incidence of severe adverse events. Notably, the GEMRITUX trial underscored the delayed therapeutic effects of rituximab, with clinical remission becoming more evident during extended follow-up periods. This further emphasizes the importance of immunologic remission as a precursor to clinical improvement [38].

Rituximab appears to be a valuable therapeutic option for pediatric patients with SRNS, particularly those with CNI-resistant forms. However, its efficacy may be influenced by the timing of its administration and prior treatment regimens. Ongoing research is needed to optimize treatment protocols and assess long-term outcomes [37,38].

Eculizumab

This monoclonal antibody targeting complement protein C5 has demonstrated significant effectiveness in treating atypical hemolytic uremic syndrome (aHUS), particularly in cases where uncontrolled complement activation leads to renal and systemic organ damage. It works by inhibiting the terminal complement pathway, preventing the formation of the membrane attack complex, which is central to the progression of thrombotic microangiopathy (TMA), a hallmark of aHUS [39,40].

In clinical trials, eculizumab has shown impressive results in improving hematologic parameters, such as platelet count and lactate dehydrogenase levels, and significantly reducing the need for plasma exchange or dialysis. For instance, in one phase 2 study, 88% of patients achieved hematologic normalization at the 1-year follow-up, with similar outcomes maintained at the 2-year mark. Furthermore, renal function improvements were observed, with patients showing stabilization or enhancement in their estimated glomerular filtration rate (eGFR) [39,41].

The efficacy of eculizumab has been consistently demonstrated across diverse patient populations, including those with chronic kidney disease resulting from aHUS. Notably, eculizumab has also been applied to treat post-transplant aHUS recurrences, with positive outcomes such as sustained kidney function and the avoidance of graft loss. Despite its high cost, the long-term benefits of eculizumab, particularly its ability to prevent disease progression and improve quality of life, make it a critical therapy in managing aHUS [40].

However, one primary safety concern is the increased risk of meningococcal infections due to complement inhibition. This risk is mitigated through mandatory vaccination and prophylactic antibiotic treatments. The ongoing clinical use of eculizumab, coupled with evolving guidelines and further studies, continues to solidify its role as a first-line therapy for aHUS [39,41].

Daratumumab

This monoclonal antibody targeting CD38 has demonstrated significant effectiveness in treating a range of refractory kidney diseases, particularly those involving immune dysregulation, such as lupus nephritis (LN) and membranous nephropathy (MN). By selectively depleting CD38+ plasma cells, daratumumab modulates the immune response, reducing the production of pathogenic autoantibodies that contribute to renal inflammation and damage. Its mechanism of action involves not only depletion of plasma cells but also the modulation of other immune cells, thereby inhibiting the progression of kidney injury associated with these conditions [42].

In clinical studies, daratumumab has shown promising results, particularly in refractory LN, where it has significantly reduced proteinuria and improved kidney function. For example, in a case series of six patients with refractory LN, five achieved a clinical response, with three patients reaching complete renal remission. Furthermore, daratumumab treatment was associated with a reduction in anti-double-stranded DNA (dsDNA) antibodies and markers of immune activation, including interferon-gamma (IFN-γ) and soluble B cell maturation antigen (sBCMA). These results suggest that daratumumab effectively modulates the immune system, providing long-term benefits in disease control [42,43].

The use of daratumumab has also extended to other nephrological conditions, such as MN and antibody-mediated rejection (AMR) in kidney transplantation, where it has been shown to reduce donor-specific antibodies (DSAs) and improve graft survival. In patients with multi-drug-resistant MN, daratumumab treatment rapidly decreased anti-PLA2R antibodies, resulting in improved renal function and reduced proteinuria. Similarly, in transplant patients experiencing AMR, daratumumab helped stabilize kidney function and reduced the need for further immunosuppressive therapies [42,43].

Despite its promising results, the use of daratumumab is associated with some safety concerns. The most common side effects are infusion-related reactions, including fever, chills, and dyspnea. Additionally, there is a risk of hypogammaglobulinemia, which can predispose patients to infections. These risks are typically managed with pre-treatment with corticosteroids and careful monitoring during therapy. However, the benefits of daratumumab, particularly its ability to induce remission in refractory kidney diseases, outweigh the risks, making it a valuable therapeutic option for patients unresponsive to conventional treatments [42,43].

Daratumumab has proven to be a highly effective and well-tolerated treatment for various refractory kidney diseases, including lupus nephritis, membranous nephropathy, and antibody-mediated rejection in kidney transplant recipients. Its ability to modulate the immune system and deplete pathogenic plasma cells offers a novel approach to treating these complex conditions. Although further studies are required to confirm its long-term

safety and efficacy, daratumumab is emerging as a critical therapy in the management of these challenging nephrological diseases [42,43].

Isatuximab

This anti-CD38 monoclonal antibody has emerged as a potential treatment for refractory kidney diseases, including membranous nephropathy (MN), lupus nephritis (LN), and in the context of kidney transplantation. This monoclonal antibody works by targeting and depleting CD38+ plasma cells, which are involved in the production of pathogenic antibodies in autoimmune conditions. Like daratumumab, isatuximab has demonstrated effective results through various mechanisms, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC), and antibody-dependent cellular phagocytosis (ADCP) [42].

Isatuximab has shown potential as a therapeutic option for refractory kidney diseases, including membranous nephropathy (MN) and lupus nephritis (LN). In MN, it has been proposed as an alternative for patients who do not respond to traditional treatments like rituximab and corticosteroids, with studies indicating that it significantly reduces anti-phospholipase A2 receptor (PLA2R) antibodies, which play a key role in MN's pathogenesis. This reduction is associated with improved renal function and decreased proteinuria. In LN, where relapses often occur despite intensive immunosuppressive therapy, isatuximab targets plasma cells responsible for producing autoantibodies, such as anti-dsDNA, potentially reducing inflammation and kidney damage in patients resistant to conventional treatments. Additionally, isatuximab is being investigated in kidney transplantation as part of desensitization protocols for highly sensitized patients, showing promise in reducing donor-specific antibodies (DSAs) and enhancing transplant success rates [42].

While clinical trials are ongoing, the results indicate that isatuximab is a promising addition to treating refractory kidney diseases, particularly in patients with MN and LN. Its ability to modulate the immune response and target plasma cells positions it as a valuable tool in managing autoimmune-related kidney conditions and enhancing outcomes in kidney transplantation. However, further studies are required to establish its long-term safety and efficacy and its optimal use in combination with other therapies [42].

Adalimumab

This fully human monoclonal antibody that targets tumor necrosis factor-alpha (TNF-α) has been extensively studied for its potential in treating nephrological conditions, particularly diabetic nephropathy (DN) and focal segmental glomerulosclerosis (FSGS).

In diabetic nephropathy, a study involving animal models demonstrated that adalimumab significantly reduced both blood glucose levels and urinary albumin, markers of kidney injury. Moreover, the treatment attenuated inflammatory cytokines such as TNF-α, MCP-1, and NF-kB in renal tissue. These findings suggest that adalimumab can potentially halt the progression of DN by modulating the TNF-α signaling pathway. The study emphasized that TNF-α plays a pivotal role in DN pathogenesis, particularly in promoting glomerular damage and proteinuria. The positive results in animal models support the consideration of adalimumab as a potential treatment for DN [44,45].

Similarly, in the context of FSGS, adalimumab has been evaluated in clinical trials, including the FONT (Novel Therapies for Resistant FSGS) study. FSGS is a complex kidney disorder that often leads to end-stage kidney disease, with many patients being resistant to standard treatments like corticosteroids and immunosuppressive drugs. In the FONT study, patients treated with adalimumab did not achieve the primary endpoint of a 50% reduction in proteinuria, a key marker of kidney function improvement. This outcome contrasted with some earlier studies, including those from the FONT-I trial, where some patients showed some improvement in proteinuria after adalimumab treatment. The FONT study did suggest that genetic and molecular profiling of FSGS patients, particularly those with TNF-α activation, could help identify those who may benefit more from TNF-α inhibitors like adalimumab. While the trial did not demonstrate widespread success with adalimumab in FSGS, it highlights the complexity of the disease and the need for personalized treatment approaches [45].

Studies underline the promising role of adalimumab in modulating inflammation and potentially altering the disease course in nephrology. However, its efficacy in FSGS remains inconclusive, requiring more targeted research into patient selection, genetic markers, and a better understanding of the disease mechanisms. Despite these challenges, the results from DN studies and the preliminary findings from FSGS trials advocate for further investigation into TNF-α inhibition as a therapeutic strategy in nephrology.

Table I. Therapeutic Monoclonal Antibodies in Renal Diseases: Mechanisms and Clinical Impact

Name	Mechanism	Investigated conditions	Potential Effect
Sibeprenlimab	Humanized IgG2 monoclonal antibody targeting a Proliferation-Inducing Ligand (APRIL - CD256).	IgA nephropathy	Slowing disease progression and preserving renal function, delaying or preventing the onset of end-stage renal disease (ESRD).
Obinutuzumab	A type II IgG1 subclass monoclonal antibody targeting CD20.	Steroid-resistant nephrotic syndrome, glomerulonephritis - mainly membranous nephropathy (MN) and lupus nephritis	Reducing proteinuria in resistant nephrotic syndromes, extending remission periods, and reducing the need for additional corticosteroids and immunosuppressants.
Secukinumab	A fully human monoclonal antibody targeting interleukin-17A (IL-17A).	Lupus nephritis	Reducing renal inflammation and subsequent fibrosis while preserving immune function, thereby minimizing the adverse effects associated with conventional immunosuppressive therapies.
Rituximab	A chimeric monoclonal antibody targeting CD20.	Membranous glomerulonephritis (MGN), steroid-resistant nephrotic syndrome (SRNS)	Reducing proteinuria, improving renal function, and enhancing overall renal outcomes.
Eculizumab	A monoclonal antibody targeting complement protein C5.	Atypical hemolytic uremic syndrome (aHUS)	Enhancing hematologic parameters, including platelet count and lactate dehydrogenase levels, while significantly reducing the need for plasma exchange or dialysis and stabilizing or improving estimated glomerular filtration rate (eGFR). A key safety consideration is the elevated risk of meningococcal infections associated with complement inhibition.
Daratumumab	A monoclonal antibody targeting CD38.	Lupus nephritis (LN), membranous nephropathy (MN), antibody-mediated rejection (AMR) in kidney transplantation	Reducing proteinuria and improving kidney function while modulating the immune system to achieve long-term disease control. Regulating donor-specific antibodies (DSAs) to enhance graft survival. Stabilizing kidney function and minimizing the need for additional immunosuppressive therapies in transplant recipients with antibody-mediated rejection (AMR). However, the most common adverse effects include infusion-related reactions such as fever, chills, and dyspnea. Additionally, there is a risk of hypogammaglobulinemia, which may increase susceptibility to infections.
Isatuximab	A monoclonal antibody targeting CD38.	Membranous nephropathy (MN), lupus nephritis (LN), kidney transplantation	Enhancing renal function and reducing proteinuria while mitigating inflammation and kidney damage in patients resistant to conventional therapies. Lowering donor-specific antibodies (DSAs) to improve transplant success rates.
Adalimumab	A monoclonal antibody targeting tumor necrosis factor-alpha (TNF-α).	Diabetic nephropathy (DN), focal segmental glomerulosclerosis (FSGS)	Lowering blood glucose levels and urinary albumin while attenuating inflammatory cytokines such as TNF-α, MCP-1, and NF-κB in renal tissue, suggesting a potential role in halting the progression of diabetic nephropathy (DN). However, efficacy in focal segmental glomerulosclerosis (FSGS) remains inconclusive, necessitating further research.

Belimumab	A fully human monoclonal antibody targeting B-lymphocyte stimulator (BLyS).	Lupus nephritis	Enhancing renal outcomes, preserving kidney function, and achieving sustained proteinuria control while maintaining a favorable safety profile.
Tocilizumab	A humanized monoclonal antibody targeting the interleukin-6 receptor (IL-6R).	Antibody-mediated rejection (ABMR) after kidney transplantation, kidney transplant recipients infected with COVID-19	Reducing donor-specific anti-HLA antibodies, improving histologic lesions associated with antibody-mediated rejection (ABMR), and stabilizing kidney function in patients resistant to standard therapies. Modulating the cytokine storm in kidney transplant recipients with COVID-19. Enhancing long-term graft survival by inhibiting memory B-cell maturation and preventing alloantibody rebound.
Fresolimumab	A humanized monoclonal antibody targeting all three isoforms of transforming growth factor-beta (TGF-β).	Focal segmental glomerulosclerosis (FSGS)	Reducing proteinuria and stabilizing kidney function, thereby mitigating fibrotic progression. Optimizing efficacy while minimizing systemic effects may require targeted delivery to fibrotic sites.
Daclizumab	A humanized monoclonal antibody targeting the alpha subunit (CD25) of the interleukin-2 receptor (IL-2R).	Kidney transplantation	No longer in clinical use due to safety concerns, but played a significant role in shaping targeted immunomodulatory strategies in renal transplantation.
Abatacept	A CTLA-4 Ig fusion protein targeting CD80/CD86–CD28 costimulatory pathway.	Minimal change disease (MCD)	Achieving long-term remission in a patient with steroid- and calcineurin-dependent minimal change disease (MCD), significantly reducing the frequency and severity of relapses while facilitating the tapering of concurrent immunosuppressants and maintaining a favorable tolerability profile.

Discussion

The use of mAbs already represents a significant advancement in treating diseases traditionally managed with immunosuppressive and cytotoxic therapies.

Monoclonal antibodies represent significant advancements in the treatment of those conditions. Rituximab, introduced in the late 1990s, has been a cornerstone of targeted therapy for several decades, providing a more precise approach than traditional broad-spectrum immunosuppressants. Its use has demonstrated efficacy in conditions resistant to conventional treatments [46]. However, obinutuzumab is a more recent and innovative mAb representing a newer generation of targeted therapies. It incorporates advanced engineering to enhance its effectiveness and reduce the risk of adverse effects [12-18].

Traditional therapies, including corticosteroids, immunosuppressants, and cytotoxic agents such as cyclophosphamide and azathioprine, have been used for several decades. For instance, corticosteroids have been a cornerstone of therapy since the 1950s, and immunosuppressive agents like azathioprine were introduced in the 1960s [47,48]. In the management of diseases such as IgA nephropathy or membranous nephropathy, these therapies have remained the standard for over 50 years. However, these treatments are often associated with incomplete efficacy and significant toxicity [48].

Traditional therapies are also well known for their broad systemic effects, often leading to serious complications. Long-term corticosteroid use, for instance, can result in hypertension, diabetes, osteoporosis, and an increased risk of infection [49]. Cytotoxic agents are notorious for their risk of malignancies, infertility, and bone marrow suppression [50]. In comparison, mAbs are associated with fewer off-target adverse effects, reduced potential for drug-drug interactions, higher specificity, and potentially increased efficacy through their focused therapeutic mechanisms [51]. Using mAbs also facilitates corticosteroid-sparing regimens, which help mitigate the long-term complications typically associated with

corticosteroid therapy. Unlike traditional treatments, which often require complex dosing schedules and frequent monitoring to prevent toxicity, mAbs are generally administered intravenously at extended intervals, for example, a few weeks. This prolonged dosing interval simplifies the treatment regimen and reduces the frequency of hospital visits, decreasing the overall treatment burden on patients and healthcare systems. Early clinical trials of mAbs and published case reports have demonstrated improved disease remission rates and fewer relapses [5,14].

Conclusion

Within a few years of their introduction into clinical practice, monoclonal antibodies (mAbs) have significantly advanced treatment regimens for many diseases, including IgA nephropathy, lupus nephritis, and glomerular diseases presenting with nephrotic syndrome. The prominent examples include sibeprenlimab, obinutuzumab, and secukinumab, which have shown promising treatment outcomes. Research has demonstrated that sibeprenlimab, a humanized IgG2 monoclonal antibody targeting a Proliferation-Inducing Ligand (APRIL) used in the treatment of IgA nephropathy, leads to a reduction in proteinuria and stabilization of eGFR. Obinutuzumab has proven effective in treating steroid-resistant nephrotic syndrome and autoimmune glomerulonephritis, such as membranous nephropathy and lupus nephritis. It also contributed to reducing the need for additional corticosteroids and immunosuppressants. The inclusion of secukinumab, a fully human monoclonal antibody targeting IL-17A, in lupus nephritis treatment regimens has led to reduced inflammation and progressive renal fibrosis, without suppressing the entire immune system.

Other antibodies have also shown therapeutic potential across various renal diseases. Belimumab, targeting B-lymphocyte stimulator (BLyS), improved renal outcomes in lupus nephritis and helped preserve kidney function. Tocilizumab, an IL-6 receptor antagonist, has been utilized in antibody-mediated rejection and desensitization protocols in kidney transplantation. Fresolimumab, by inhibiting TGF-β, has been evaluated in focal segmental glomerulosclerosis (FSGS), providing a novel approach to fibrosis reduction. Daclizumab, targeting IL-2Rα, has served as induction therapy in transplantation, although it is no longer in use. Abatacept, a CTLA-4 Ig fusion protein, has demonstrated effectiveness in minimal change disease by targeting CD80. Rituximab remains a key therapy for steroid-resistant nephrotic syndrome and membranous nephropathy, with proven long-term efficacy. Eculizumab, inhibiting complement C5, is now a first-line therapy for atypical hemolytic uremic syndrome due to its effect on thrombotic microangiopathy and renal preservation. Daratumumab and isatuximab, both anti-CD38 antibodies, have shown promise in refractory lupus nephritis, membranous nephropathy, and antibody-mediated rejection, providing targeted plasma cell depletion. Lastly, adalimumab, a TNF-α inhibitor, has demonstrated immunomodulatory effects in diabetic nephropathy and focal segmental glomerulosclerosis.

Early clinical trials of mAbs, along with published case reports, have shown improved disease remission rates and fewer relapses. The ability of mAbs to reduce complications associated with long-term corticosteroid use may also extend patients' life expectancy and improve their quality of life. By more effectively targeting the underlying disease mechanisms, mAbs may offer the potential for durable remissions and enhanced preservation of organ function. However, the long-term effects of monoclonal antibody therapies are still being investigated. Whether they will significantly improve overall survival across all patient groups remains to be seen. Some patients may still require a combination of traditional therapies and mAbs for optimal disease control.

Conflict of interest
None
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