

Targeting B cells in immune-mediated kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

Jürgen Floege¹, Isabelle Ayoub², Silke R. Brix^{3,4,5}, Kirk N. Campbell⁶, Richard Furie⁷, Patrick H. Nachman⁸, Sydney C.W. Tang⁹, Nicola M. Tomas^{10,11}, Marina Vivarelli¹², Michael Cheung¹³, Jennifer M. King¹³, Morgan E. Grams¹⁴, Michel Jadoul¹⁵ and Brad H. Rovin¹⁶; for Conference Participants¹⁷

¹Department of Nephrology & Rheumatology, University Hospital, Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen, Aachen, Germany; ²Division of Nephrology, The Ohio State University, Columbus, Ohio, USA; ³Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust, Manchester, UK; ⁴Renal, Transplantation and Urology Unit, Manchester University NHS Foundation Trust, Manchester, UK; ⁵Division of Cell Matrix Biology and Regenerative Medicine, University of Manchester, Manchester, UK; ⁶Division of Renal-Electrolyte and Hypertension, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA; ⁷Division of Rheumatology, Northwell Health, Donald and Barbara Zucker School of Medicine at Hofstra-Northwell, Great Neck, New York, USA; ⁸Division of Nephrology and Hypertension, University of Minnesota, Minneapolis, Minnesota, USA; ⁹Division of Nephrology, Department of Medicine, School of Clinical Medicine, University of Hong Kong, Hong Kong, China; ¹⁰III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ¹¹Hamburg Center for Kidney Health (HCKH), University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ¹²Nephrology Research Unit and Clinical Trial Center, Bambino Gesù Children's Hospital IRCCS, Rome, Italy; ¹³KDIGO, Brussels, Belgium; ¹⁴Department of Medicine, New York University Langone School of Medicine, New York, New York, USA; ¹⁵Division of Nephrology, Cliniques Universitaires Saint Luc, Université Catholique de Louvain, Brussels, Belgium; and ¹⁶Division of Nephrology, Department of Internal Medicine, The Ohio State Wexner Medical Center, Columbus, Ohio, USA

Treatments that deplete or modulate B cells are in use or being investigated for several immune-mediated glomerular diseases. Kidney Disease: Improving Global Outcomes (KDIGO) convened a Controversies Conference in Panama City, Panama, in June 2025 to review current evidence and identify key gaps in knowledge and research needs to effectively apply such therapies. Availability, effectiveness, and safety of B cell-targeted therapies vary substantially across glomerular diseases. In IgA nephropathy, anti-CD20 therapy (rituximab) has shown limited efficacy, although inhibitors of survival factors BAFF (B cell activating factor) and APRIL (a proliferation-inducing ligand) and anti-CD38 antibodies can lead to reduction in proteinuria and reduction in decline in estimated glomerular filtration rate. In contrast, for membranous nephropathy, anti-CD20 antibodies have become first-line therapy, achieving at least partial remission in most patients by 18 months. In steroid-dependent nephrotic syndrome, rituximab effectively prevents relapses, particularly in children, though benefits are transient. For

lupus nephritis, newer approaches including obinutuzumab and chimeric antigen receptor (CAR) T cell therapy have shown promising results, with CAR T cells introducing the possibility of being free of disease activity and treatment for a prolonged time. In antineutrophil cytoplasmic antibody-associated glomerulonephritis, rituximab has proven effective for both induction and maintenance therapy, with ongoing trials investigating CAR T cell approaches. Safety considerations of B cell-targeting therapies vary by intensity of therapy, with conventional anti-CD20 therapy showing favorable safety profiles and CAR T cell therapy requiring careful patient selection because of the potential for cytokine release syndrome and other serious adverse events. Validating biomarkers for patient selection and monitoring is a critical research need, along with optimizing treatment protocols and determining optimal therapy duration.

Kidney International (2026) ■, ■-■; <https://doi.org/10.1016/j.kint.2026.02.029>

KEYWORDS: autoimmune; B cells; biomarkers; glomerulonephritis

© 2026 Kidney Disease: Improving Global Outcomes (KDIGO). Published by Elsevier Inc. on behalf of the International Society of Nephrology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Correspondence: Jürgen Floege, Department of Nephrology & Rheumatology, University Hospital, Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen, Pauwelsstr. 30, 52074 Aachen, Germany. E-mail: jfloege@ukaachen.de; or Brad H. Rovin, Ohio State University Nephrology, 1654 Neil Avenue, Fourth Floor, Columbus, Ohio, USA. E-mail: brad.rovin@osumc.edu

¹⁷Additional Conference Participants are listed in the [Appendix](#).

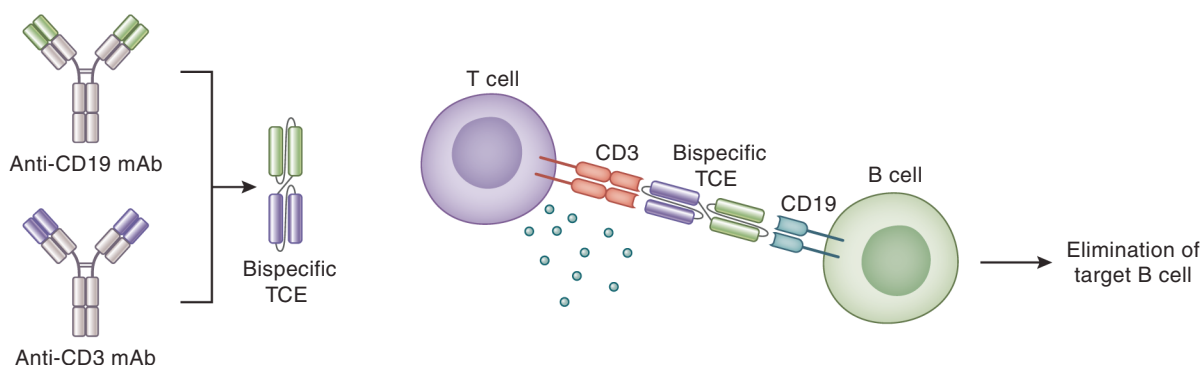
Received 5 February 2026; revised 13 February 2026; accepted 26 February 2026

Recent clinical trials using biologics or cell therapies that deplete or modulate B cells have enhanced clinical responses across immune-mediated glomerular diseases. Despite the early failure of rituximab in lupus nephritis (LN),¹ using anti-CD20 monoclonal antibodies for

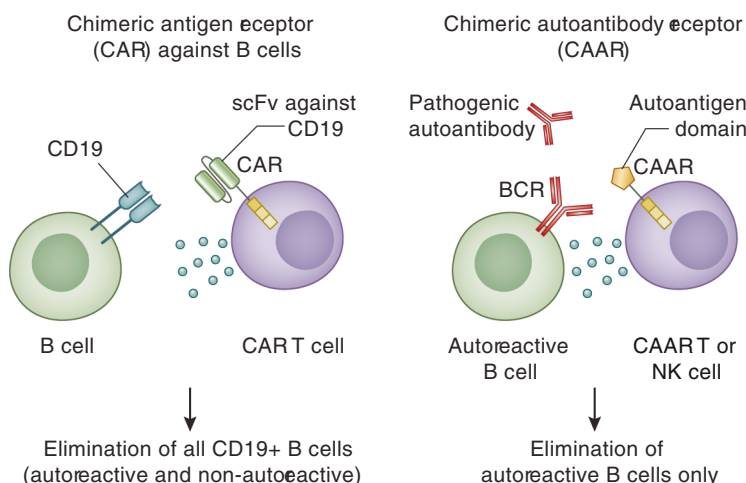
depleting B cells has become commonplace for managing podocytopathies,^{2,3} membranous nephropathy (MN), vasculitis, and LN.^{4,5} Monoclonal antibodies against the B cell growth and survival factors BAFF (B cell activating factor) and APRIL (a proliferation-inducing ligand) and anti-CD38 plasma cell antibodies have shown robust effects on proteinuria and glomerular filtration rate (GFR) stability in phase II to III IgA nephropathy (IgAN) trials. Chimeric antigen receptor (CAR) T cells constructed to bind and kill B lineage cells that express CD19 and/or B cell maturation antigen (BCMA) may change treatment paradigms for autoimmune diseases such as LN and have introduced the concepts of *deep B cell depletion*, *immunologic reset*, and even *cure*. A key question is whether deep B cell depletion is due to the greater breadth of B-lineage cells being depleted by CD19 and/or BCMA CAR T, or because CAR T cells achieve more complete peripheral and lymphoid tissue B

cell depletion, or both. Trailing closely behind cell therapy in development are the T cell engagers, uniquely constructed antibodies that redirect the host's T cells to kill B cells or other specific cells of the host immune system (Figure 1).^{6,7} Although these biologics and cell therapies offer the opportunity to titrate the level of B cell depletion, several issues need further clarification. These include the risk-benefit ratio and the required depth and method of B cell modulation and depletion for specific glomerular diseases and an individual's disease manifestations. To address these issues, adult and pediatric nephrologists, rheumatologists, pathologists, hematologists/cell therapists, B cell scientists, and patients with glomerular disease were assembled in Panama City, Panama, in June 2025 for the Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference on Therapies Targeting B Cells in Immune-Mediated Kidney Diseases.

a Principle of bispecific T cell engager (TCE) action



b CAR and CAAR principles for targeting B cells



c CAR constructs

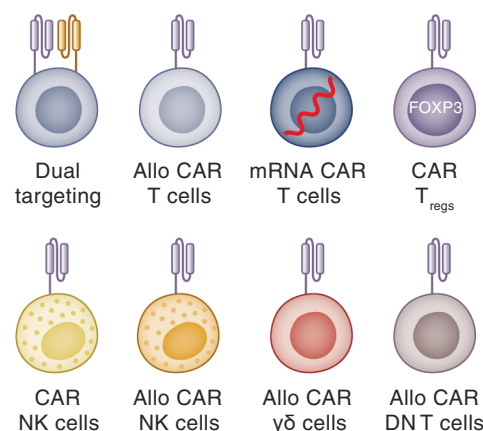


Figure 1 | Strategies for deep B cell depletion. (a) Principle of bispecific T cell engager (TCE) action using a nonantibody base. (b) Chimeric antigen receptor (CAR)-based approaches include the simultaneous targeting of multiple antigens, the use of autologous or allogeneic T cells to generate CAR T cells, mRNA-based genetic modification leading to transient expression of CARs, and the use of alternative cellular backbones such as regulatory T cells (T_{regs}), natural killer (NK) cells, $\gamma\delta$ T cells, and CD3+ CD4/CD8 double-negative (DN) T cells (as shown in (c)). Chimeric autoantibody receptor (CAAR) T cells are engineered with a receptor that mimics the structure of an autoantigen and specifically binds to B cells and CD19+ plasma cells that express surface autoantibodies responsible for the production of pathogenic autoantibodies. BCR, B cell receptor; mAb, monoclonal antibody; scFv, single-chain variable fragment. (c) Reproduced with permission from Mougiakakos D, Meyer EH, Schett G. CAR T cells in autoimmunity: game changer or stepping stone? *Blood* 2025; 145:1841–1849.⁸

Rationale for targeting B cells in glomerular diseases

Many—maybe most—glomerular diseases are driven, at least in part, through (auto)antibodies. These secreted antibodies found in serum may arise in the setting of autoimmunity or may be normally present but altered or overproduced, may be directly pathogenic, or may activate other arms of the immune system to induce kidney injury.

A recent review of B cell and plasma cell biology has revealed the importance of long-lived, nonreplicating CD19+ plasma cells as possible key players in autoimmune disease. Contrary to popular belief, the vast majority of plasma cells in the human body are CD19+, including two-thirds of plasma cells in the bone marrow.^{9,10} These CD19+ plasma cells are not short-lived plasmablasts; in the bone marrow <5% of both CD19+ and CD19− plasma cell subsets express the proliferation marker Ki-67,⁹ and both subsets may live for years to decades (reviewed in Suan *et al.*¹¹). Like short-lived plasmablasts and CD19− plasma cells, CD19+ plasma cells do not express CD20. Because CD19 is the cell surface reporter for paired box protein 5 (PAX5), the master transcription factor for the B cell program, these CD19+ plasma cells are also B cells, highlighted by their coexpression of surface Ig and major histocompatibility complex II. While functioning normally as plasma cells to secrete soluble antibody, CD19+ plasma cells may simultaneously perform the operations of a B cell: capturing antigen, presenting peptide-major histocompatibility complex II to CD4+ T cells, and clonally proliferating. Of note, secreted autoantibody in circulation may or may not be pathogenic, but the surface autoantibody on B cells and CD19+ plasma cells may be pathogenic by turning these cells into key autoantigen-presenting cells that activate CD4+ T cells. The recognition of this numerically dominant population of long-lived CD19+ CD20− plasma cells, which also function as B cells, provides one explanation for the differences observed between targeting CD20 and CD19 for depletion in autoimmune disease.¹¹

Eliminating or suppressing B cells and/or plasma cells has emerged as a very appealing treatment strategy for glomerular diseases. This Controversies Conference was focused on IgAN, MN, podocytopathies, LN, and antineutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA GN), as the pathogenesis of these glomerular diseases represents the breadth of antibody-mediated kidney injury.

IgA nephropathy. IgAN is an immune-mediated disease believed to be driven by altered gut and respiratory tract mucosal responsiveness, increased circulation of galactose-deficient IgA1 (Gd-IgA1) and likely other pathogenic IgA species, and cross-reactive anti-pathogen antibodies plus pathogenic autoantibodies (anti-Gd-IgA1 IgG and IgA autoantibodies) through oligoclonal expansion of autoantibody-producing cells. Increased BAFF and APRIL levels are associated with increased circulating levels of Gd-IgA1 and anti-Gd-IgA1 antibodies in IgAN,¹² and genetic loci encoding APRIL and its cognate B cell receptor transmembrane activator and calcium modulator and

cyclophilin ligand interactor are risk loci for IgAN.¹³ These B cell-associated factors contribute to the formation, circulation, and deposition of IgA-containing immune complexes in glomeruli, leading to progressive injury.¹⁴

Membranous nephropathy. MN is a classical autoimmune disease characterized by glomerular subepithelial Ig and complement deposition.^{15,16} The identification of multiple autoantigens has led to a new antigen-based classification of MN.^{17–19} Experimental studies verified that antibodies against M-type phospholipase A2 receptor (PLA2R) or thrombospondin type-1 domain-containing 7A (THSD7A) induce typical manifestations of MN.^{20–25} In addition, emergence of anti-PLA2R autoantibodies may predict disease development²⁶ or relapse, and disappearance of anti-PLA2R autoantibodies precedes disease remission.²⁷ Higher antibody levels correlate with an increased risk of loss of kidney function, disease relapse, and disease recurrence after kidney transplantation as well as a lower likelihood for remission.^{27–33}

Podocytopathies. Podocytopathies are characterized by pronounced, often nephrotic proteinuria and podocyte damage on biopsy. The classic examples are minimal change disease and focal segmental glomerulosclerosis (FSGS).³⁴ Until recently, minimal change disease had been considered a T cell-mediated disease, and FSGS was thought to be due to a circulating “permeability” factor, possibly derived from lymphocytes. Importantly, an FSGS pattern of injury can also be seen in diseases caused by genetic variations in podocyte proteins, and FSGS is a final common pathway of other glomerular injuries resulting in nephron loss. The idea that at least some podocytopathies could be mediated by B cells grew from observations that children and adults—mostly with minimal change disease but some with FSGS—responded to treatment with the B cell-depleting agent rituximab. The recent identification of anti-nephrin antibodies in adults and, more frequently, children with immunosuppression-responsive podocytopathies has now provided a possible explanation for these observations (Table 1).^{35–41} In addition, proteinuria and podocyte injury developed in a rabbit after transfer of anti-nephrin IgG from a patient with minimal change disease, suggesting a pathogenic role of anti-nephrin autoantibodies.⁴² Antibodies directed against other podocyte proteins, that is, podocin and Kirrel1 (kirre-like nephrin family adhesion molecule 1),⁴³ have since been described. Finally, levels of memory B cells have been shown to predict disease relapse in children.^{44–47} Taken together, these findings suggest that at least some podocytopathies may be effectively treated with anti-B cell agents.

Systemic autoimmune diseases that affect the kidneys: LN and ANCA-associated vasculitis. The pathogenesis of systemic lupus erythematosus (SLE) involves most of the components of the immune system but seems to begin with loss of tolerance to self-antigens, possibly related to ineffective disposal of cellular debris.⁴⁸ Circulating autoantibodies to endogenous self-antigens are present in patients destined to develop SLE years before clinical disease is apparent.⁴⁹ As

Table 1 | Anti-nephrin antibodies in different forms of podocytopathy

Study	Detection method	Population	Positivity rate	Additional findings
Watts <i>et al.</i> ³⁵	Immunoprecipitation + signal-enhanced ELISA (laboratory nephrin-ECD-His)	MCD 41 children /21 adults (NEPTUNE)	18/62 (29%)	Shorter relapse-free in anti-nephrin (+)
Hengel <i>et al.</i> ³⁷	Immunoprecipitation or hybrid immunoprecipitation/ELISA (laboratory nephrin-ECD-His)	INS 182 children MCD 105 adults Primary FSGS 74 adults Secondary FSGS 40 adults	INS 94/182 (52%) MCD 46/105 (44%) Primary FSGS 7/74 (9%) Secondary FSGS 1/40 (3%)	Correlation of proteinuria with anti-nephrin titers Increased prevalence in IST naive
Raglianti <i>et al.</i> ⁴¹	Standard ELISA (commercial RDnephrin-ECD-His)	MCD/FSGS 12 children SSNS 13 children MCD/FSGS 19 adults	MCD/FSGS 4/12 (33%) SSNS 5/13 (38%) MCD/FSGS 2/19 (11%)	Super-resolution microscopy showed colocalization with nephrin
Hengel <i>et al.</i> ³⁸	Immunoprecipitation (laboratory nephrin-ECD-His)	INS 333 children SSNS 101 SDNS 67 Nongenetic SRNS 103 Genetic SRNS 62	SSNS 69/101 (68%) SDNS 19/67 (28%) Nongenetic SRNS 14/103 (14%) Genetic SRNS 1/62 (2%)	Higher prevalence in active disease Positive nongenetic SDNS 18% response versus 0% negative
Shirai <i>et al.</i> ³⁶	Signal-enhanced ELISA (commercial RDnephrin-ECD-His)	FSGS 8 Nongenetic FSGS transplant 14 (11 recurrence)	Recurrent 11/11 (100%) Nonrecurrent 1/3 (33%)	
Batal <i>et al.</i> ³⁹	Signal-enhanced ELISA (laboratory nephrin-ECD-his)	MCD/FSGS transplant 38 (21 recurrence) <i>Before transplant</i>	Recurrent 8/21 (38%) Nonrecurrent 0/17 (0%)	(+) Anti-nephrin HR 4.29 (IQR, 1.25–18.8) for recurrence
Shu <i>et al.</i> ⁴⁰	Standard ELISA IgG/IgM-validated WB and microscopy (commercial SB nephrin-ECD-His)	MCD 436 Primary FSGS 160	MCD 196/436 (45%) (30% IgG/27% IgM/12% both) Primary FSGS 60/160 (37.5%) (29% IgG/24% IgM/16% both)	Higher prevalence active disease Positive > nephrotic syndrome Positive > relapse/frequent relapse Decreased at remission

ELISA, enzyme-linked immunosorbent assay; FSGS, focal segmental glomerulosclerosis; HR, hazard ratio; INS, idiopathic nephrotic syndrome; IQR, interquartile range; IST, immunosuppressive therapy; MCD, minimal change disease; nephrin-ECD-His, extracellular domain of nephrin fused to a polyhistidine tag; NEPTUNE, Nephrotic Syndrome Study Network; RD, R&D Systems; SB, Sino Biological; SDNS, steroid-dependent nephrotic syndrome; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome; WB, Western blot.

autoantibodies accumulate in patients with SLE and their repertoire of target antigens expands, clinical disease ensues. LN develops in ~50% of patients with SLE owing to glomerular immune complex accumulation, activation of the complement system, and recruitment of leukocyte populations. The glomerular location of the immune complexes determines the subsequent histology of the LN (e.g., mesangial, membranous, and proliferative).

In contrast, ANCA GN is characterized by a pauci-immune glomerulonephritis, usually in the presence of circulating antibodies directed against myeloperoxidase (MPO) or proteinase 3 (PR3) present in the granules of neutrophils and lysosomes of monocytes. These antibodies activate neutrophils that have been primed to express MPO

or PR3 on their surface, resulting in a respiratory burst that generates toxic oxygen free radicals and degranulation, initiating vasculitis. Glomerular and alveolar capillaries are particularly vulnerable to this injury, leading to glomerulonephritis and pulmonary hemorrhage, respectively.

Lessons from the application of B cell–directed therapies to glomerular diseases

B cell therapeutics tool box. An overview of established and emerging approaches discussed during the conference can be found in [Table 2](#)^{11,50–53} and [Figure 1](#).⁸

IgAN. In an open-label multicenter trial, rituximab did not significantly decrease proteinuria or affect kidney function over 12 months, nor did it reduce levels of Gd-IgA1 or

Table 2 | Established and emerging approaches of therapies targeting B cells

Agent	Description and comments
Glucocorticoids, antimetabolites, and cytotoxic drugs	Can deplete or affect the function of B cells,⁵² but are not targeted B cell therapies and broadly affect other immune cell types, leading to a wide range of adverse events.
B cell–modulating agents	- Neutralize BAFF, APRIL, or BAFF plus APRIL. - BAFF binds to BCMA, TACI, and BAFF receptors on B cells and plasma cells; APRIL binds to BCMA and TACI receptors.⁵¹ - BAFF inhibition impairs B cell maturation; APRIL does not. Both decrease Ig production, but APRIL is more selective for IgA than IgG. - APRIL inhibition may affect plasmablast and plasma cell differentiation, trafficking, and survival. - The BAFF inhibitor belimumab has been approved for treatment of LN.⁵⁰ - Anti-APRIL monoclonal antibodies (sibeprenlimab and zigakibart) or TACI receptor–IgG fusion proteins that block the effects of BAFF and APRIL (atacept, telitacept, and povetacept) are being investigated mainly in IgAN. - The anti-APRIL monoclonal antibody sibeprenlimab has been approved for the treatment of IgAN.
Type I CD20 antibodies	- Anti-CD20 antibodies kill naive, germinal center, and memory B cells. - Rituximab kills B cells through complement and ADCC. - Used on-label to treat ANCA GN and off-label in IgA vasculitis, MCD, FSGS, MN, and LN. - Neutralized after cellular internalization through lipid rafts.
Type II CD20 antibodies	- Kill B cells through ADCC and programmed cell death, which do not require complement and are not internalized, so tend to be more potent than type I antibodies. - Obinutuzumab has been approved for the treatment of LN.
CD19 antibodies	- Extend the range of B cell and plasma cell subsets that are depleted to CD20– B lineage cells (e.g., short-lived plasmablasts and long-lived CD19+ plasma cells, but not very long-lived CD19 – plasma cells that mostly reside in the bone marrow).^{9,11} - Inebilizumab is being investigated in LN in a phase II study (ClinicalTrials.gov Identifier: NCT06570798).
CD38 antibodies and other agents	Monoclonal antibodies directed toward CD38 (daratumumab, felzartamab, and mezagitamab) and small molecules (bortezomib) kill both short-lived plasmablasts and long-lived plasma cells.
CAR T cells directed against B cells and CD19+ plasma cells (CD19–CAR T cells) or B cells plus all plasma cells (CD19–BCMA CAR T cells)	- Currently being applied mainly to autoimmune diseases including LN. - Most programs use autologous cells; allogeneic and <i>in vivo</i> CAR T cell choices are emerging.⁵³ - Trial results raise new concepts such as depth of B cell depletion, immune reset, and the possibility of cure. - Need to determine the appropriate level of B cell depletion for an individual patient, given the choice of B cell therapies that result in different levels of depletion.
Bispecific antibodies and T cell engagers	- Engineered bispecific antibodies can be made, for example, to bind CD3 on T cells and CD19, CD20, or BCMA on B and plasma cells. - Binding B and T cells simultaneously allows the activated T cell to kill the B cell or plasma cell. - Conceptually like cell therapy without the need for cell infusions. - Range of adverse events due to activation of T cells and B cell killing is similar to those due to cell therapies. - Blinatumomab is being investigated in LN in a phase II study (ClinicalTrials.gov Identifier: NCT06570798).

ADCC, antibody-dependent cytotoxicity; ANCA GN, antineutrophil cytoplasmic antibody–associated glomerulonephritis; APRIL, a proliferation-inducing ligand; BAFF, B cell activating factor; BCMA, B cell maturation antigen; CAR T cell, chimeric antigen receptor T cell; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; LN, lupus nephritis; MCD, minimal change disease; MN, membranous nephropathy; TACI, transmembrane activator and calcium modulator and cyclophilin ligand interactor.

its corresponding autoantibodies.⁵⁴ Because plasma cells, which are not depleted by anti-CD20 treatment, likely produce Gd-IgA1 and anti-Gd-IgA1 antibodies, plasma cell depletion with proteasome inhibition or anti-CD38 monoclonal antibodies was tried in IgAN. Plasma cell depletion decreased proteinuria and slowed the rate of GFR decline.^{55–57} Similarly, recent studies investigating anti-APRIL antibodies (such as sibeprenlimab^{58,59} and zigakibart⁶⁰) and dual BAFF/APRIL inhibitors (including atacicept,^{61–63} telitacicept,⁶⁴ and povetacicept⁶⁵) showed that compared with placebo, these B cell modulators decreased Gd-IgA1 and anti-Gd-IgA antibodies, reduced proteinuria, and slowed the rate of estimated glomerular filtration rate (eGFR) loss to levels comparable with physiologic decline during the treatment period. Despite overall reductions in serum IgA, IgG, and IgM, there was no increase in adverse events, including infections. However, upon treatment discontinuation, Gd-IgA1 levels rebounded toward baseline levels, suggesting that long-term suppression with these agents may be needed.^{58,66}

In summary, peripheral depletion of CD20-expressing B cells is not sufficient to control IgAN. These results do not exclude the possibility that an anti-CD20 agent with better tissue B cell depletion or an anti-CD19 agent that broadens the scope of B cells depleted to include plasmablasts and CD19+ plasma cells could be effective. Very deep B cell depletion by CAR T cells, natural killer cells, or T cell engagers has not yet been tested in IgAN but may be of interest in treatment-refractory cases, where medication nonadherence or other injurious conditions have been excluded. A clinical trial from mainland China using CD19-CAR T cell therapy ([ClinicalTrials.gov](#) Identifier: NCT06690359) is underway in adults with biopsy-proven IgAN. If the phase II GFR slope data for APRIL and BAFF/APRIL inhibition are replicated in phase III trials, there may be no rationale for additional or combination therapy for IgAN, as achieving a physiologic rate of eGFR decline represents an optimal outcome and goal. Patients treated with a B cell modifier who continue to experience a decline in eGFR of >1 ml/min/yr may need additional therapy, possibly guided by kidney biopsy. It is even conceivable that foundational antiproteinuric chronic kidney disease agents, such as renin-angiotensin system blockers, may no longer be necessary in this context, even though this seems unlikely in the presence of advanced chronic kidney disease.

Membranous nephropathy. Anti-CD20 antibodies have become the first-line therapy for most patients with MN, and single agent treatment appears to be sufficient for the majority of patients requiring immunosuppressive therapy to attain at least partial remission by 18 months.^{4,67–75} Obinutuzumab, a more potent anti-CD20 antibody than rituximab, has been successfully used, mainly in refractory MN.^{76–78} It remains to be seen whether obinutuzumab has advantages over rituximab, particularly in rapidity, completeness, and duration of response. A phase III randomized controlled trial

(RCT) ([ClinicalTrials.gov](#) Identifier: NCT04629248) testing obinutuzumab versus tacrolimus for MN is underway. A preliminary study of ofatumumab, a fully human anti-CD20 monoclonal antibody with strong complement-dependent cytotoxicity, revealed promising results, mainly in patients with refractory or complicated MN.⁷⁹

Depending on the origin of autoantibodies in MN (CD19+ or CD19– plasma cells), an anti-CD19 monoclonal antibody may offer an advantage over anti-CD20 antibodies and/or may be similar to treatment with a combination of anti-CD20 and plasma cell inhibition.

Plasma cell-directed therapy with the anti-CD38 monoclonal antibody felzartamab was tested in an exploratory phase II trial in patients with PLA2R-associated MN with relapsing and refractory disease⁸⁰ and led to a rapid decline in anti-PLA2R levels in most patients and a decline in proteinuria of ≥50% in 35% of patients. Therapy was generally well-tolerated.

Combination B cell therapies are only beginning to be studied in MN. Because B cell depletion with anti-CD20 antibodies causes a rise in BAFF levels, which may promote the maturation of undepleted autoreactive B cells, an RCT exploring the combined use of “sandwich” belimumab-rituximab-belimumab in comparison to rituximab alone is underway ([ClinicalTrials.gov](#) Identifier: NCT03949855).⁸¹ Other potential therapies being explored for MN include inhibitors of either APRIL or BAFF plus APRIL, and phase I/II study data of a BAFF/APRIL inhibitor were promising.⁸² All the RCTs of rituximab in MN show that anti-PLA2R antibody levels decline within several weeks.^{4,83} A proof-of-concept observational study evaluated the combination of plasmapheresis followed by an anti-CD20 agent with a goal to accelerate the reduction of anti-PLA2R antibodies.⁸⁴ This begs the question of whether a more rapid response for patients with MN may be achieved by using anti-CD38 therapy to rapidly reduce anti-PLA2R, followed by anti-CD20 therapy.

Although there is great enthusiasm over the potential of CAR T cell therapies for autoimmune diseases,^{85–87} MN is typically not a rapidly progressive disease, does not usually require chronic immunosuppressive therapy, affects an older patient population that may be less able to tolerate CAR T cell therapy, and is rarely truly treatment-resistant. Thus, CAR T cell therapies are not felt to address an “urgent” unmet need in the treatment of MN and would be considered only for patients with severe nephrotic syndrome who fail to respond to anti-B cell therapy as well as to second-line treatment with cyclophosphamide and glucocorticoids. At the same time, the field is evolving rapidly. To further enhance treatment specificity and reduce adverse effects, application of more tolerable approaches may become an option for MN, and these may include “off-the-shelf” allogeneic CAR T cells, *in vivo* CAR T cells,⁵³ or CAR natural killer cells⁸⁸ or the use of antigen-specific strategies (e.g., exclusively targeting anti-PLA2R autoantibody-producing cells) ([Figure 1](#)).^{89,90} A CD19XCD3 bispecific antibody is

currently being trialed in MN ([ClinicalTrials.gov](#) Identifiers: NCT07234474 and NCT06982729), but results are not yet available.

Podocytopathies. In children, B cell depletion with anti-CD20 antibodies is effective for preventing relapses of steroid-dependent nephrotic syndrome (SDNS)^{91,92}; however, the evidence for rituximab to induce remission at initial disease presentation is lacking.^{92,93} A meta-analysis of RCTs in children with SDNS/frequently relapsing nephrotic syndrome comparing rituximab with conventional immunosuppressive therapy showed that rituximab significantly increased short-term complete remission rates and long-term complete remission rates with some reduction in cumulative glucocorticoid dose and improvement in linear growth, albeit no significant differences in severe adverse events.⁹⁴ However, the benefit of rituximab is transient and retreatment protocols remain to be established.⁹⁵ In severe forms of SDNS, the sequential use of mycophenolate mofetil after rituximab has been shown to prolong the time to relapse.⁹⁶ Importantly, rituximab is less effective in severe childhood nephrotic syndrome⁹⁷ and in children younger than 10 years.⁴⁶ This may be because during the first 10 years of life, memory B cells are still developing and reconstitute more rapidly after B cell depletion.⁹⁸ The fully humanized anti-CD20 antibody ofatumumab has similar efficacy as rituximab.⁹⁹ Obinutuzumab was associated with remission in pediatric case reports¹⁰⁰ and is currently being compared in RCTs with mycophenolate mofetil ([ClinicalTrials.gov](#) Identifier: NCT05627557, phase II) and rituximab ([ClinicalTrials.gov](#) Identifier: NCT05786768, phase II–III).

In adults with SDNS/frequently relapsing nephrotic syndrome, case series and observational studies demonstrate a role for B cell depletion with rituximab in inducing complete remission (albeit with variable efficacy), decreasing the number of relapses, and prolonging the duration of remission.^{101–105} There are some published data evaluating initial anti-CD20 use in adults, mostly in small case series with variable efficacy for achieving complete remission.^{106,107}

Belimumab, an anti-BAFF monoclonal antibody, was not effective in a small study of children with frequently relapsing nephrotic syndrome.¹⁰⁸ Combination therapies of B cell depletion with anti-CD20 antibodies (rituximab, obinutuzumab) and plasma cell depletion with anti-CD38 antibodies (daratumumab) have been successfully used in some adults and children with treatment-resistant nephrotic syndrome or relapsing FSGS post-transplant.^{109–112}

Although the identification of anti-nephrin and other anti-podocyte antibodies raises the intriguing possibility of very deep (tissue) B cell depletion including plasma cells as a possible therapeutic approach, anti-nephrin positivity has been associated with the most benign, treatment-responsive, steroid-sensitive conditions³⁸ that are least in need of more aggressive treatment options. Nonetheless, very deep B cell depletion could have a role in very severe cases, for example,

recurrent FSGS post-transplant or severe multi-drug-dependent patients, especially in cases with comorbidities related to prolonged and intense immunosuppression.

Lupus nephritis. In LN clinical trials, therapies targeting B cells have been added to standard-of-care (SOC) immunosuppressive regimens, usually either cyclophosphamide or mycophenolate mofetil plus glucocorticoids.^{1,3,50,113,114} Belimumab provided a significant benefit to patients with LN over SOC alone and was approved for LN in 2020.⁵⁰ Rituximab was similarly tested against SOC and failed in a phase III RCT.¹ However, patients who demonstrated peripheral B cell depletion with rituximab experienced a kidney remission advantage compared to SOC.¹¹⁵

Exploring the possibility that intensified B cell depletion would improve outcomes of anti-CD20 treatment, obinutuzumab was studied in LN. The phase II NOBILITY trial ([ClinicalTrials.gov](#) Identifier: NCT02550652) showed that nearly all patients treated with obinutuzumab achieved peripheral B cell depletion and had more complete kidney responses than did those treated with placebo.¹¹⁴ B cell depletion by obinutuzumab is not limited to circulating cells. In a study of sensitized patients with kidney failure who were treated with obinutuzumab in preparation for kidney transplantation, lymph node biopsies were performed and showed B cell depletion.¹¹⁶ A phase III trial of obinutuzumab in proliferative LN (REGENCY, [ClinicalTrials.gov](#) Identifier: NCT04221477) recently read out. The complete kidney response rate of patients treated with obinutuzumab in REGENCY was 13.1% higher than that of patients treated with placebo, leading to the drug's approval by the US Food and Drug Administration and European Medicines Agency for the treatment of proliferative LN in 2025.³ In addition to complete peripheral B cell depletion in almost every obinutuzumab-treated patient, a subset of patients from REGENCY had a kidney biopsy after 18 months of treatment; B cells were absent from the kidneys of patients who received obinutuzumab but were present and unchanged from baseline kidney biopsies in patients who received placebo.¹¹⁷ The successes of obinutuzumab compared with rituximab are likely explained by its intensified peripheral and tissue-level B cell depletion.¹¹⁸

Belimumab added to SOC has been endorsed as a first-line LN treatment by the KDIGO 2024 Clinical Practice Guideline for the Management of Lupus Nephritis¹¹⁹ and the 2024 American College of Rheumatology Guideline for the Screening, Treatment, and Management of Lupus Nephritis.¹²⁰ The 2025 LN guideline from the European Alliance of Associations for Rheumatology endorsed belimumab or obinutuzumab plus SOC as a first-line LN therapy.¹²¹

Therapies targeting plasma cells have been used in small uncontrolled studies of patients with refractory LN. Bortezomib treatment was given to 12 patients with LN who did not respond to several standard immunosuppressive regimens and resulted in 1 complete kidney response and 10 partial responses.¹²² Because of toxicity concerns with

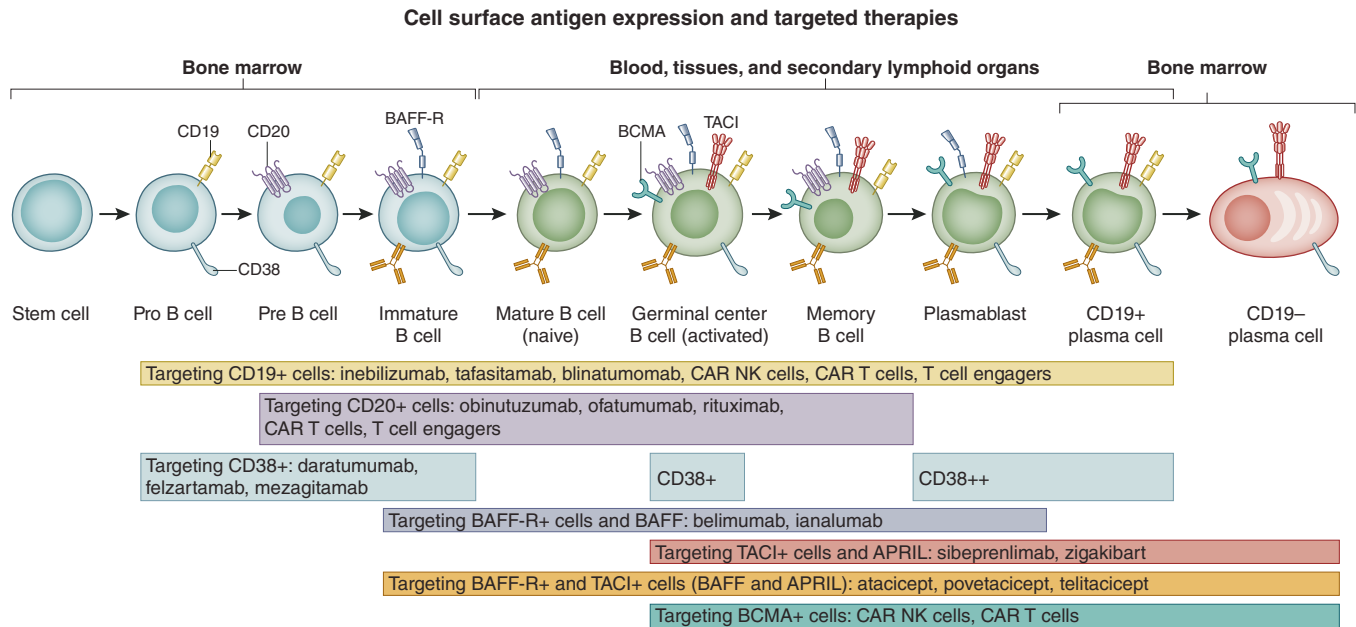


Figure 2 | B cell maturation, treatment targets, and therapies. APRIL, a proliferation-inducing ligand; BAFF, B cell activating factor; BAFF-R, B cell activating factor receptor; BCMA, B cell maturation antigen; CAR, chimeric antigen receptor; CAR NK, chimeric antigen receptor natural killer; Pro, progenitor; TACI, transmembrane activator and calcium modulator and cyclophilin ligand interactor.

bortezomib, plasma cell depletion was studied using anti-CD38 antibodies, which did induce responses in several patients with refractory LN.^{123,124} The use and positioning of plasma cell therapies in LN remains to be defined.

CAR T cell therapies directed against CD19 or CD19 and BCMA (Figure 2) demonstrated impressive short- and long-term resolution of LN in a small phase I study¹²⁵ and a case series.⁸⁵ The CAR T cell therapies were administered after all other immunosuppressive medications, including glucocorticoids and anti-malarial agents, had been stopped. However, to create an environment favorable to the expansion of infused CAR T cells, a lymphodepleting regimen, usually consisting of cyclophosphamide and fludarabine, is routinely administered; its contribution, if any, to the clinical outcomes is not known. In addition to yielding kidney response outcomes far better than those seen with conventional B cell-directed therapies, many patients have remained in immunosuppressive-free remission for up to 2 years after a single infusion of CD19-CAR T cells.⁸⁵

In summary, intensified B cell depletion may provide better LN response results, and it is possible CD19 offers improved benefits over CD20 as a target because targeting CD19 depletes a larger number of B cell phenotypes that may retain autoimmune memory. Deep B cell depletion includes an absence of circulating B cells as well as depletion of B cells in lymphoid tissues and, possibly, the kidney (Figures 3 and 4). This is accomplished to some extent by obinutuzumab but to a greater extent by cell therapies. In addition, an early return of a naïve B cell phenotype (CD20+, CD27–, IgD+, and IgM+) has been observed with CAR T cell

therapy, raising the possibility that cell therapies may reset the immune system in autoimmunity.⁸⁷

ANCA-associated vasculitis. B cell depletion with rituximab has become central in ANCA-associated vasculitis (AAV) induction and maintenance therapy, reducing cyclophosphamide use and replacing azathioprine for long-term maintenance immunosuppression. Different intensities and frequencies of rituximab administration achieve differing results, reinforcing the concept that the extent of B cell depletion may determine treatment efficacy.¹²⁸ Currently, there are no trial data on obinutuzumab, although it is used as rescue treatment in patients with therapy-resistant disease.¹²⁹ Unlike for LN, the B cell modifier belimumab failed to prevent flares of AAV in the Belimumab in Remission of VASculitis (BREVAS) study.¹³⁰

Case reports demonstrate induction of complete remission in patients with treatment-refractory MPO and PR3 AAV treated with CD19-CAR T cells.^{131,132} Phase I and II trials are underway to investigate CAR T cell therapy directed against CD20+ cells in AAV, and research aims to selectively target autoreactive MPO and PR3 ANCA-producing cells.

Expectations of treatment

Cure. Although there have always been patients with autoimmune disease who respond well to treatment with conventional therapies and became disease-free off medications, most patients achieve alternative outcomes (discussed later). “Cure” entered the vernacular after the introduction of CAR T cell therapy, specifically in LN. The LN and AAV discussion group at this conference defined *cure* as the

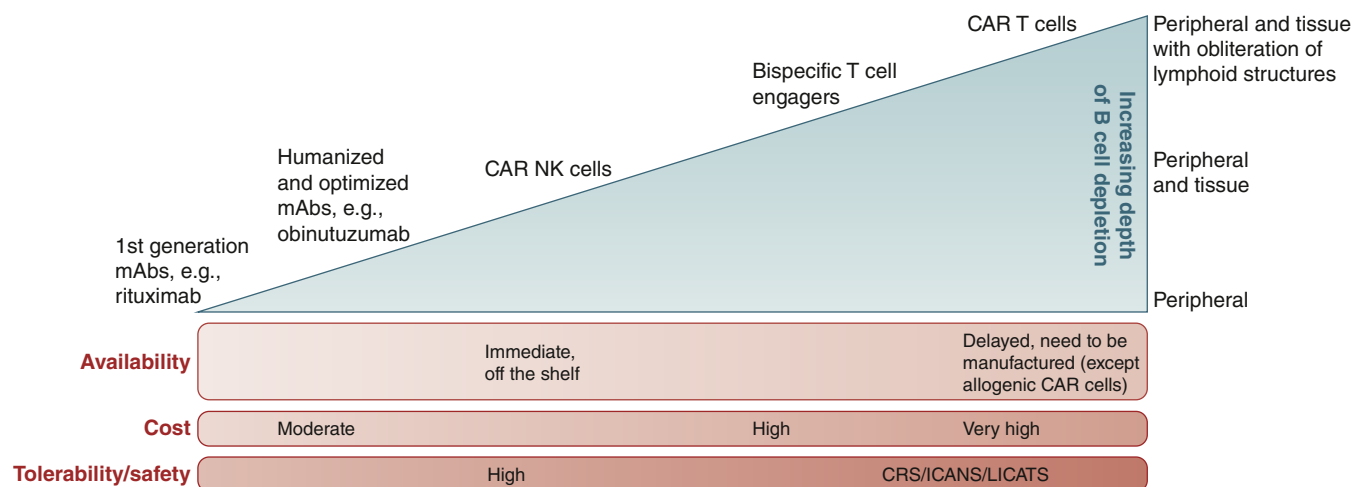


Figure 3 | Depth and breadth of B cell depletion via various therapies in kidney disease. The various agents targeting B cells and their depth of B cell depletion peripherally and in tissue along with factors related to treatment availability, cost, and toxicity. CAR NK cell, chimeric antigen receptor natural killer cell; CAR T cell, chimeric antigen receptor T cell; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LICATS, local immune effector cell-associated toxicity syndrome; mAb, monoclonal antibody.

absence of clinical, immunologic, and histologic signs of disease activity while the patient is off all immunosuppressive therapies. Simply put, cure is a reversion of the immune system to the premorbid state when medications were unnecessary. There was no consensus about the minimum duration of medication-free disease activity to declare cure, but a patient's lifetime was considered ideal.

Although safety is not an element of the definition of cure, it must be considered when assessing the benefit of a therapeutic intervention. A curative treatment that poses a significant safety risk may be less appealing to patients and clinicians than a safer therapy that may not be curative.

Alternative outcomes to cure. Cure as defined above will likely be an infrequent event for the foreseeable future and is therefore aspirational. Short of lifelong cure, being free of disease activity, or being off treatment for at least a few years was considered a clinically meaningful treatment outcome and attainable. For example, several patients with refractory lupus responded to CAR T cell therapy and have remained disease free off all immunosuppressive therapies for up to 2 years.⁸⁵ *Activity-free disease* implies immunologic, histologic, and clinical resolution. Determination of clinical resolution may be straightforward, but histologic and immunologic resolution are more nuanced. To avoid the need for repeat kidney biopsies, the availability of noninvasive biomarkers that reflect kidney pathology will be critical (discussed later). Immunologic resolution may not equate with disappearance of autoantibodies, given the observation that some patients with autoimmune diseases achieve complete response after CAR T cell therapy despite persistence of autoantibodies.^{85,133}

The concept of being free of disease activity and free of treatment can be applied generally to other glomerular or autoimmune diseases. In a few children with podocytopathies, the use of anti-CD20 therapy after glucocorticoid-

induced remission has been disease-modifying, inducing prolonged remission off therapy. Patients with MN who have complete remission of proteinuria can often be treatment-free for years. In AAV, immunosuppression can often be held after maintenance therapy with rituximab. In contrast, it is not clear whether IgAN treatment can achieve this composite outcome goal. For example, B cell-modulating therapies seem to stabilize GFR, but presumed signs of disease activity, such as presence of Gd-IgA1 and anti-Gd-IgA1, return quickly after the BAFF/APRIL or APRIL inhibitors are stopped.^{58,66} Thus, for some glomerular diseases, an outcome of absence of disease activity while on treatment may be a reasonable treatment outcome, especially if ongoing therapy is well-tolerated.

Biomarkers to guide the implementation and monitoring of B cell therapies in glomerular diseases

IgA nephropathy. It is unlikely that every patient with IgAN needs B cell therapy to achieve disease remission (i.e., stable eGFR and minimal to no proteinuria). Guiding patient selection for B cell-targeting therapies using only proteinuria and eGFR is too crude, and there are no validated histologic biomarkers. Furthermore, even if tissue B cells could serve as a biomarker for choosing a B cell therapy in IgAN, the relevant tissue of interest for analyzing B cells is unclear and could include the kidney, gut mucosa, regional (gut and kidney) lymph nodes, or even tonsils.

Gd-IgA1 and anti-Gd-IgA1 antibodies are often discussed as biomarkers for identifying patients who may respond to B cell treatment, but validated and standardized clinical assays are lacking, as are prospective studies showing that they, or total IgA, can guide selection for B cell treatment. Finally, Gd-IgA1 levels in patients with IgAN are modestly elevated above normal, and substantial overlaps exist between patients and healthy controls.¹³⁴ Mass spectrometry confirmed that sialylation of IgA1 O-glycans was associated with

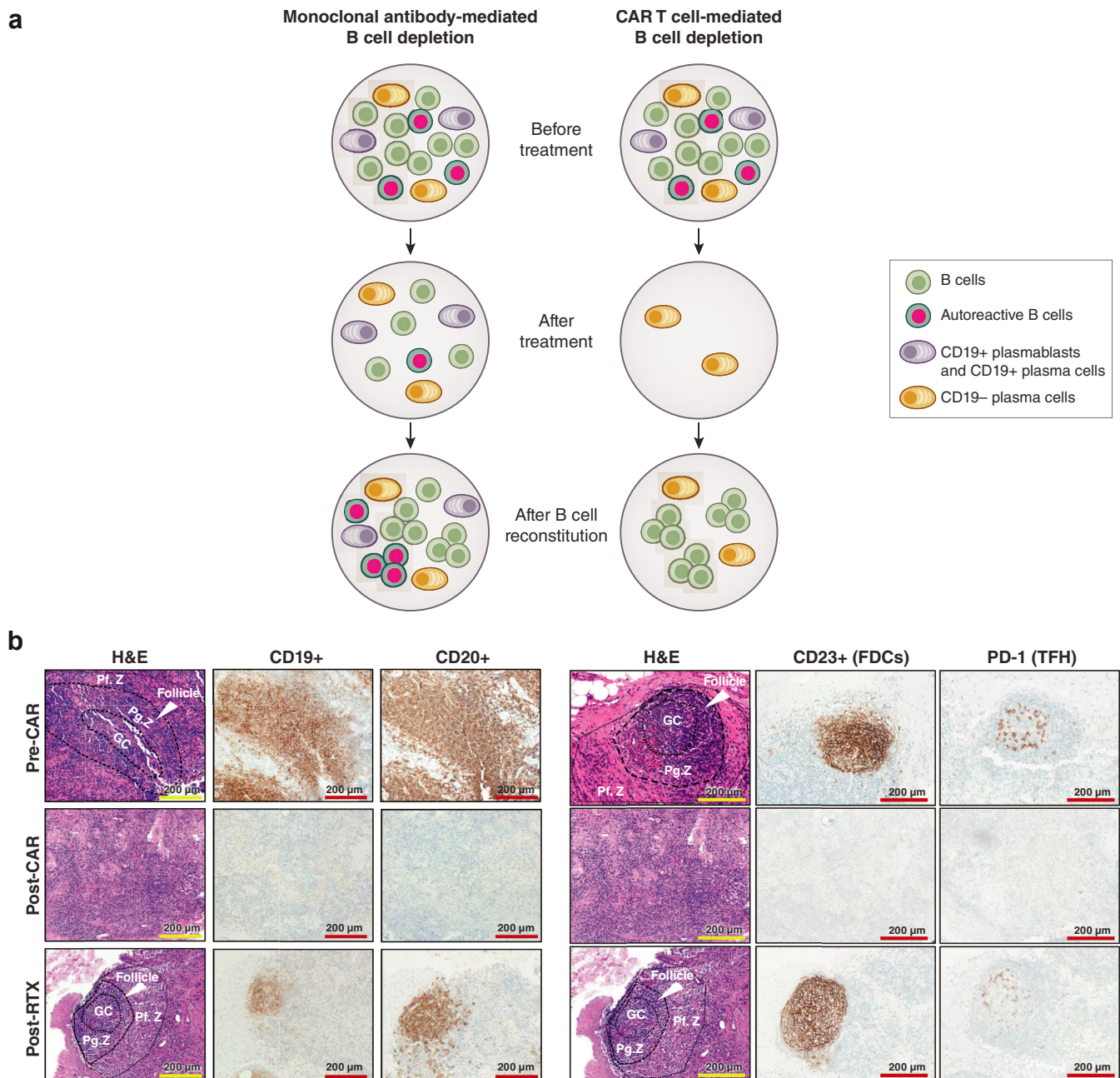


Figure 4 | Comparison of B cell depletion by monoclonal antibodies and cell therapies. (a) Effects of antibody-based and cell-based B cell targeting in autoimmune disease. Pretreatment, autoreactive B cells and plasmablasts are interspersed in a larger number of alloreactive B cells and plasmablasts. Posttreatment, *in situ* autoreactive and alloreactive B cells are reduced but not eradicated with antibody-mediated B cell depletion; plasmablasts and plasma cells are not depleted by anti-CD20 monoclonal antibodies; CD19-CAR (chimeric antigen receptor) T cells lead to a deep depletion of autoreactive and alloreactive B cells, plasmablasts, and CD19+ plasma cells without reducing CD19- plasma cells. During B cell reconstitution after anti-CD20 monoclonal antibody-mediated B cell depletion, autoreactive and alloreactive B cells are replenished. CD19-CAR T cell therapy autoimmune B cell clones and plasmablasts remain absent. (b) Peripheral blood and lymph node changes on CD19-CAR T cell therapy. Left: Representative hematoxylin and eosin (H&E)-stained images of lymph node biopsies obtained from 1 patient treated before (pre-CAR) and after (post-CAR) CD19-CAR T cell therapy and from 1 patient after RTX therapy (post-RTX), together with representative immunohistochemistry images of CD19+ B cells and CD20+ B cells. White arrows indicate follicular B cell areas in the lymph node tissue. Right: Changes in the B cell maturation compartment in the lymph nodes. Representative H&E-stained images of lymphoid follicles/germinal centers pre-CAR and post-CAR as well as post-RTX, together with representative immunohistochemistry images of CD23+ follicular dendritic cells (FDCs) and programmed cell death protein 1+ (PD-1+) T follicular helper cells (TFHs). GC, germinal center; Pf. Z, peri-follicular zone; Pg.Z, peri-germinal zone. (a) Reproduced with permission from Schett G, Nagy G, Krönke G, et al. B-cell depletion in autoimmune diseases. *Ann Rheum Dis* 2024;83:1409–1420.¹²⁶ (b) Reproduced with permission from Tur C, Eckstein M, Velden J, et al. CD19-CAR T-cell therapy induces deep tissue depletion of B cells. *Ann Rheum Dis*. 2025;84:106–114.¹²⁷

IgAN¹³⁵; however, there is substantial overlap in glycosylation patterns between IgAN and controls. The levels of autoantibodies or cross-reactive antibodies (IgG or IgA) targeting Gd-IgA1 also overlap with healthy controls.¹³⁴ All recent trials of B cell modulators reduced Gd-IgA1, total IgA, and IgG levels, indicating a nonspecific rather than targeted reduction in Ig production.

Several other potential targets of B cell therapies are exploratory, untested, or unvalidated as biomarkers in the setting of IgAN, such as tertiary lymphoid structures¹³⁶ or IgA class-switched CD27–CD21+ B cells/IgA+ plasmablasts.¹³⁷

Membranous nephropathy. In anti-PLA2R-positive MN, it is assumed most patients who need treatment will be offered a B cell therapy. Although patients with the highest tertile anti-PLA2R antibody levels often require immunosuppressive treatment, spontaneous proteinuria remission is common in patients with the lowest tertile of anti-PLA2R antibody levels.³³ The clinical utility of the non-anti-PLA2R autoantibodies in guiding treatment of MN is currently unknown, but it seems likely that at least anti-THSD7A antibodies behave similarly to anti-PLA2R antibodies.^{18,138}

Measuring circulating CD19– or CD20+ B cells after the use of an anti-B cell agent is recommended, but whether there is a role for monitoring B cell repopulation in deciding when or whether to repeat dosing of these agents is currently unknown. The measurement of B cell subsets (naïve, double negative, CD38+, transitional, or memory) for prognostic or disease monitoring purposes¹³⁹ is not available outside of research settings. Measuring antigen-specific B cells, which could be the best indicators of ongoing immunological disease activity, should be explored in future research.

Podocytopathies. For immunological biomarkers, changes in certain lymphocyte subpopulations, that is, increased circulating memory B cells and plasmablasts and decreased regulatory T cells, in children^{140–143} and adults^{144,145} have been linked to immune-responsive (especially steroid-dependent) forms of nephrotic syndrome. According to a retrospective analysis of a large cohort of patients with SDNS/frequently relapsing nephrotic syndrome, baseline total memory and switched memory B cells before anti-CD20 therapy were independently associated with a small but statistically significant increased risk of subsequent relapse.⁴⁶ In the pediatric setting, post-rituximab reconstitution of switched memory B cells was likewise associated with a significantly increased risk of relapse, independent of ethnicity.^{44,45,47} Promising approaches for finding better biomarkers include more sophisticated deep lymphocyte phenotyping, such as single-cell RNA sequencing¹⁴⁶ and elucidating the role of B cells directly in disease-relevant tissues (kidney, lymph nodes, spleen, tonsils, etc.) (Figure 4). Consistent with previous findings, single-cell RNA sequencing analyses have also identified the recovery of memory B cells as a predictor of post-rituximab response.¹⁴⁶ However, because this association has only been found in observational studies,

it requires validation in prospective clinical trials before clinical implementation.

The pathogenic role of anti-podocyte protein antibodies is supported in murine models by passive transfer of autoantibodies⁴² and by direct immunization with recombinant nephrin.³⁷ In humans, circulating anti-nephrin titers are low, and detection techniques have proved technically challenging and difficult to reproduce.^{147–149} Some very preliminary data have shown anti-podocyte antibody negativity in remission and after rituximab treatment both in native kidney disease^{36,37} and after kidney transplantation.¹⁵⁰

Systemic autoimmune diseases. In LN, there are neither predictive biomarkers to guide clinicians in the selection of initial therapy nor monitoring biomarkers to indicate response to treatment. Studies in individuals with LN have yet to correlate changes in anti-double-stranded DNA titers with clinical response. In contrast, complement factors have predictive power; for patients treated with mycophenolate mofetil or cyclophosphamide, normalization of C3 and C4 by week 8 is predictive of kidney response at week 24.¹⁵¹ Entry into clinical trials evaluating deep B cell-depleting regimens (CAR T cells or bispecific antibodies) has been entirely based on the disease being refractory to prior therapies.

In ANCA GN, it is assumed that most patients will be treated with a B cell-depleting agent (anti-CD20) alone or in combination with cyclophosphamide as initial therapy. The ANCA antibody subtype associates with relapse risk, and PR3 ANCA is generally regarded as carrying a higher relapse risk.^{5,152,153} After treatment, ANCA levels are expected to fall or disappear; ANCA persistence and reoccurrence after B cell depletion seems to confer a higher relapse risk in patients with PR3 and MPO.^{153,154} Seroconversion of ANCA from negative to positive therefore warrants close monitoring for relapse, but there is insufficient evidence that autoantibody reappearance mandates retreatment.^{152,155}

Given the growing number of B cell-directed agents and their likely future use in ANCA GN and LN, it will be crucial to monitor B cell depletion, repletion, and modulation. Peripheral blood B cell numbers and subsets after therapy and during recovery can be measured, but the CAR T cell trial experience suggests that outcomes depend on the depth of B cell depletion in the tissue, not in the periphery (Figure 3).^{126,127} It would be ideal to measure B cells in tissue, but the acquisition of lymphoid tissue, such as lymph nodes or tonsils, poses a challenge, and serial kidney biopsies to assess B cell tissue kinetics are not feasible. A promising and relatively noninvasive technique to assess B cell depletion, including germinal center B cells in tissues, uses nasal-associated lymphoid tissue acquired from the nasal cavity by swabbing.¹⁵⁶ Somatic mutational analysis of Ig and non-Ig genes comparing memory B cells before treatment with repopulated cells may also provide an indication of the depth of B cell depletion.

What is immune reset, and is this possible and desirable? The term *immune reset*, coined after CAR T cells began to be trialed in autoimmune diseases, has become the goal of treatment for cell therapies and other agents designed

to achieve deep B cell depletion.⁸⁵ After such therapies the immune system appears to revert to a naive immune phenotype characterized by the disappearance of autoantibodies, the elimination of IgG and IgA memory B cells, and repopulation by B cells that display a naive phenotype (CD19+, CD27-) as opposed to a memory phenotype (CD19+, CD27+). Although not an official definition, the conference participants agreed that immune reset is the complete depletion of clonal autoreactive B cells and therefore deletion of B cell memory; it is a prerequisite for achieving a cure in chronic immune-mediated inflammatory conditions, such as SLE or AAV. It may also be beneficial in severe recurring forms of MN, although there is currently insufficient evidence for most forms of immune-mediated podocytopathies (excluding some recurring forms of FSGS) and for IgAN.

Although the concept of immune reset was popularized in CAR T cell studies for LN,⁸⁷ treatment with obinutuzumab in patients with LN resulted in a similar B cell repletion consisting primarily of a naive phenotype, and memory B cells were slow to return.¹¹⁴ Treatment with CD19+ CAR T cells does not completely eliminate autoantibodies. Antibodies directed against RNA-binding proteins (e.g., Smith [Sm] and Sjögren's-syndrome-related antigen A [SSA]) are not eliminated, indicating that long-lived autoreactive plasma cells, likely the CD19- subset, are not "reset."⁸⁷ In contrast to treatment with CD19+ CAR T cells, administration of bispecific anti-CD19/BCMA+ CAR T cells resulted in reductions of antibodies to both DNA- and RNA-binding proteins, suggesting plasma cells as the source of antibodies to Sm, ribonucleoprotein (RNP), SSA, and Sjögren's-syndrome-related antigen B (SSB).^{125,157-159} Conference participants discussed the controversies around the term immune reset and the necessary extent of the immune cell depletion to be considered *reset* and suggested labeling the immune phenomenon observed after CAR T cell therapy as either *immune system remodeling* or *immune system reprogramming*.

Safety considerations

B cell depletion is accompanied by an increased risk of infection, transient neutropenia, thrombocytopenia, hypogammaglobulinemia, and vaccine failure.^{3,114,160,161} A very rare complication is progressive multifocal leukoencephalopathy in patients after a John Cunningham (JC) virus (human polyomavirus 2) infection. A proportion of patients develop persistent and progressive hypogammaglobulinemia; the risk is increased in elderly patients and young children and is influenced by coadministered glucocorticoids and previous immunosuppressive burden.^{19,162} After B cell depletion, antibody titers from vaccinations may be reduced.^{19,163,164} Vaccine boosters should therefore be given when B cells reappear in the circulation. If urgent treatment with a B cell-directed therapy is needed, for example, in organ-threatening ANCA GN, delaying treatment to receive vaccination is not recommended. Attention to Ig levels, neutrophil counts, and platelet counts is imperative.

Therapies targeting plasma cells invoke yet additional precautions in that patients may require replacement i.v. Ig or a full vaccination panel if immune memory is destroyed.¹²⁵ Compared with adults, toxicity of B cell depletion, including hypogammaglobulinemia, appears to be more prevalent and profound in children, particularly those younger than 10 years.^{19,165}

Deep B cell depletion with CAR T cell therapy or bispecific antibodies in autoimmune diseases can lead to toxicities previously exclusive to patients treated for malignant neoplasms. The limited experience to date has not demonstrated a significant increase in infectious complications. However, potentially severe acute treatment-related toxicities have emerged, including cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome.¹⁶⁶ Long-term follow-up of patients treated for hematologic neoplasms has revealed that toxicities such as Parkinson disease, enteritis, and T cell lymphoproliferative disorders may occur years after CAR T cell administration.¹⁶⁷⁻¹⁶⁹ In cell therapies and bispecific antibody protocols, the risk of developing some of these syndromes may be reduced by careful patient selection. Patients with preexisting cardiopulmonary disease are at an increased risk of adverse outcomes from cytokine release syndrome. Recognition of immune effector cell-associated neurotoxicity syndrome may be challenging in patients with central nervous system lupus. It is, however, important to aim for inclusive trial platforms and not to exclude certain comorbidities such as central nervous system lupus *per se* to allow patients with an acceptable risk profile to access novel therapies. Attention needs to be paid to baseline Ig levels because patients with nephrotic syndrome may experience resolution of their initial hypogammaglobulinemia. Ongoing B cell depletion with rituximab and the accompanied loss of protective antibodies such as hepatitis B surface antibodies (anti-HBsAB) conveys viral infection risk requiring monitoring, revaccination, and antiviral prophylaxis. The relationship between the depth of B cell depletion and the absence of specific antiviral antibodies is not well understood, and determining when B cell targeting renders the patients more susceptible to particular serious infections is a research priority.

Patient and public engagement

B cell-targeted therapies, especially with CAR T cells, are more complex than prior treatments of glomerular disease. Thus, the need for patient education and shared decision making has increased significantly. There is a major concern that health professionals are not currently equipped with appropriate resources and manpower to handle these demands. Enhancing the alliance between the medical community and patient advocacy groups will offer a solution to these newfound challenges.

Cost/pharmacoeconomics. Most of the treatment approaches that target B cells in glomerular disease will undoubtedly remain very expensive and are unlikely to be available in resource-limited parts of the world for a long

Table 3 | Research priorities for therapies targeting B cells in kidney diseases**General**

- Generate biorepositories from all sponsored trials—including enrolled and screen-failed subjects within a federated biobank managed by an academic committee to facilitate data sharing, biomarker analysis, and patient profiling in glomerular diseases.
- Optimize disease phenotyping across immune-mediated glomerular diseases to select the right intensity of B cell–directed therapy for the right patient:
 - Establish clinical risk profiles.
 - Determine reliable serologic and histologic biomarkers needed to measure treatment response earlier and predict disease trajectory.
 - Repeat kidney biopsies to assess treatment response.
 - Optimize analysis of peripheral blood lymphocyte subsets to identify correlates of response and safety.
 - Acquire lymphoid tissue at the time of diagnosis and follow-up, for example, lymph nodes, bone marrow, and nasal cavity, to determine treatment algorithm.
- Establish criteria for discontinuation of B cell therapies.
- Incorporate artificial intelligence into optimizing and personalizing treatment choice and dosing.
- Determine the long-term effects of B cell depletion on immune competence and risk of malignancy.
- Define the age-specific safety profiles of B cell–depleting and –modulating agents across the lifespan of glomerular diseases.
- Define cure and immune reset specifically for each glomerular disease.
- Perform platform trials incorporating novel trial designs to overcome enrollment challenges, accelerating drug approvals.
- For complex treatment options, increase resources for patient education and involvement.

IgA nephropathy

- Examine the contribution of the change in Gd-IgA1, other potentially pathogenic IgA species, and anti-Gd-IgA1 antibody levels to eGFR preservation in completed or soon-to-be-completed trials through mediation analysis. Examine their potential role in predicting treatment response and relapses in IgAN and in determining the optimal dosing of B cell agents.
- In patients who achieve a physiologic decline in eGFR with B cell therapy, determine whether general therapies for chronic kidney disease can or should be discontinued.
- In patients who achieve a physiologic decline in eGFR with B cell therapy, determine whether residual proteinuria matters.
- Compare depth and durability of selective APRIL inhibitors versus dual BAFF/APRIL inhibitors.

Membranous nephropathy

- Characterize more completely the relationship between improvement in anti-PLA2R levels and clinical manifestations of disease including complete and partial responses.
- Characterize the natural course of non-PLA2R-associated membranous nephropathy and whether anti-PLA2R-negative patients benefit from anti-CD20 therapy.
- Optimize and personalize anti-CD20 dosing schedules and determine whether additional immunosuppressive agents are required in the context of an insufficient response to anti-CD20 treatment.
- Investigate whether earlier initiation of therapy or combination of therapeutic approaches (agents) can lead to faster remission and the prevention of complications of severe nephrotic syndrome (e.g., arterial or venous thromboembolic events)

Podocytopathies

- Explore whether B cell–depleting or –modulating agents can be used alone in adults and children as first-line therapy for podocytopathies.
- Develop biomarkers to identify who has immune-mediated disease and who will or will not benefit from B cell depletion.
- Determine whether anti-podocyte antibodies are pathogenic and/or biomarkers of disease type. Can they be used to monitor treatment response and predict response and relapse?

Lupus nephritis and ANCA-associated vasculitis

- Develop reliable biomarkers that inform therapeutic approach and are predictive of treatment response; the use of such noninvasive monitoring overcomes the circularity of the uPCR end point.
- Develop objective measures to identify those patients with trajectories warranting early escalation of B cell targeting to prevent organ failure and those patients who have achieved immune reset with therapy.
- Perform a liquid kidney biopsy to assess clinical response in the absence of tissue acquisition.
- Repeat kidney biopsies and apply novel diagnostic techniques to determine the critical point when kidney inflammation loses reversibility and results in fibrosis. Evaluate the impact of B cell depletion on fibrotic pathways.
- Determine the role of genetic predisposition and manifestations driven by other pathways, for example, IFN-1 in SLE skin disease.
- Identify the different treatment responses of vasculitic and granulomatous AAV manifestations to B cell–targeting therapies.

AAV, antineutrophil cytoplasmic antibody–associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; eGFR, estimated glomerular filtration rate; Gd-IgA1, galactose-deficient IgA1; IFN-1, interferon 1; IgAN, IgA nephropathy; PLA2R, M-type phospholipase A2 receptor; SLE, systemic lupus erythematosus; uPCR urine protein-to-creatinine ratio.

time. Furthermore, some technologies, such as cell therapy requiring manufacturing of CAR T cells, may not be present in many regions. There are no easy solutions to making new therapies available worldwide. Presently, the responsible approach for the global community interested in applying B cell therapies to glomerular diseases will be to understand who needs what level of B cell depletion and to not necessarily assume everyone needs the most expensive regimen. Learning in detail how B cell approaches work in glomerular diseases may offer insights into designing less costly approaches to treatment over time. To balance cost and safety, risk stratification for each glomerular disease should guide the depth of B cell depletion according to disease activity and severity in individual patients.

Research agenda

Research priorities resulting from this Controversies Conference are provided in [Table 3](#).

Conclusion

The role for therapeutically targeting B cells in glomerular diseases has rapidly expanded over the past decade. In IgAN, B cell modulation via APRIL and/or BAFF inhibition or via plasma cell depletion has the potential to stabilize kidney function and reduce GFR loss to levels consistent with normal aging. In MN, these advances have largely been spurred by the discovery of anti-PLA2R and other presumably pathogenic autoantibodies as well as the improved access to and use of rituximab. Autoantibodies have been and continue to be identified in patients with podocytopathies. Their pathogenicity will need to be determined. Nevertheless, in MN and in some forms of podocytopathies, the rate of complete remission remains relatively low, and the time to attain it is long. Achieving more complete and more durable remission within a shorter time frame remains an unmet need in MN and B cell-driven, treatment-dependent podocytopathies. Newer B cell-targeting agents, the use of combination therapies, and the targeting of plasmablasts and plasma cells have all shown promise in addressing this unmet need and are currently under investigation. For MN, the typical course of disease and efficacy of currently available regimens make cell-based therapies in their current form less attractive. This will likely change with the advent of newer cell-based agents as we gain more experience with CAR T cells in LN and other more rapidly progressive glomerular diseases.

In LN and ANCA GN, disease severity and individual patient factors (e.g., age, fertility, comorbidities, and frailty) are varied and necessitate broadening management beyond a *one-size-fits-all* approach. A better understanding of the tissue response to treatment will enable adapting treatment to individual patient needs. Reliable stratification models and improved monitoring methods are needed for selecting the most appropriate therapeutic interventions. Presently, cell therapies are mostly being tested in patients with refractory disease. If these therapies do provide long-term drug-free response, they may be better applied to early LN before several rounds of failed therapies to prevent chronic kidney

damage and to provide medication-free time for individuals often starting their careers and families.

Despite these advances, a significant proportion of patients with glomerular diseases develop irreversible organ damage and fail to attain long-term remission. Intensifying B cell depletion in certain patient populations may allow long-lasting disease remission off immunosuppressive therapy, moving our therapeutic goals closer to a cure of kidney diseases.

APPENDIX

Additional Conference Participants

Valeria Alberton, Argentina; Andrea Angeletti, Italy; Jennifer L. Barnas, USA; Jonathan Barratt, UK; Peter Boor, Germany; Roberto Caricchio, USA; Tak Mao Chan, Hong Kong; Eugene Yu-Hin Chan, Hong Kong; Manuela Colucci, Italy; Anne Davidson, USA; Nathan Denlinger, USA; Raphaël Duivenvoorden, The Netherlands; Marie Eggers, Germany; Alessia Fornoni, USA; Eleni Frangou, Cyprus; George E. Georges, USA; Andre G. Gontijo, USA; Shaun W. Jackson, USA; Brittan Kopittke, USA; Maria J. Leandro, UK; Nelson Leung, USA; Adrian Liew, Singapore; Ana Malvar, Argentina; Juan M. Mejia-Vilet, Mexico; Peter A. Merkel, USA; Irene L. Noronha, Brazil; Michelle M. O'Shaughnessy, Ireland; Ioannis Parodis, Sweden; Amber S. Podoll, USA; Anjay Rastogi, USA; Dario Roccatello, Italy; Jorge E. Rojas-Rivera, USA; Barbara Seitz-Polski, France; Saira Z. Sheikh, USA; Dan Suan, Australia; Rita S. Suri, Canada; Vladimír Tesar, Czech Republic; Naotake Tsuboi, Japan; Augusto Vaglio, Italy; Christoph Wanner, UK and Germany; Muh Geot Wong, Australia; Hui-Kim Yap, Singapore; Hong Zhang, China; Ming-hui Zhao, China.

DISCLOSURE

Kidney Disease: Improving Global Outcomes (KDIGO) provided travel and medical writing support to all conference participants. JF discloses receipt of consulting fees and speaker honoraria for lectures from AstraZeneca, Biogen, Boehringer Ingelheim, Calliditas Therapeutics, CSL Vifor, Novartis, Omeros, Otsuka, Roche, Sobi, STADA, Travere, Timberlyne, Vera Therapeutics, and Vertex; receipt of travel support from STADA; participation on advisory boards for AstraZeneca and Novo Nordisk; and serving in a leadership role in KDIGO. IA discloses receipt of institutional grants from Travere Therapeutics; receipt of consulting fees from Alexion, Absos Development 1 Corp, Aurinia Pharmaceuticals, Boehringer Ingelheim, Calliditas Therapeutics, GSK, Human Immunology Biosciences, Novartis, Otsuka Pharmaceuticals, Roche-Genentech, Travere Therapeutics, Vera Therapeutics, and Vertex; and receipt of speaker honoraria from Genentech and Travere Therapeutics. SRB discloses receipt of grants from the National Institute for Health and Care Research (NIHR), Vasculitis UK, and NIHR Manchester Biomedical Research Centre; receipt of consulting fees from CSL Vifor; receipt of speaker honoraria from CSL Vifor and Otsuka; receipt of travel support from CSL Vifor; advisory board participation for CSL Vifor; and serving in leadership roles in the UK and Ireland Vasculitis Rare Disease Group and European Vasculitis Society. KNC discloses receipt of consulting fees from Novartis, Otsuka, Sanofi, Travere, and Vera Therapeutics. RF discloses receipt of institutional grants from Genentech; consulting fees from GSK, Novartis, and Roche-Genentech; receipt of speaker honoraria and travel support from AstraZeneca, Chugai Pharmaceutical, GSK, and Roche-Genentech; and serving in an unpaid leadership role with the Lupus Research Alliance. PHN discloses receipt of research grants from AstraZeneca and Cabaletta Bio; receipt of royalties from *UpToDate* (Wolters Kluwer); and receipt of consulting fees from Boehringer Ingelheim, GSK, Novartis, and Q32. SCWT discloses receipt of consulting fees from Boehringer Ingelheim, Novartis, and Travere; receipt of speaker honoraria from AstraZeneca, Boehringer

Ingelheim, CSL Vifor, Everest Medicines, GSK, Novartis, Vantive, and Vera Therapeutics; and serving as a KDIGO Executive Committee member, President of the Asian Pacific Society of Nephrology, and Chair of the Publications Committee for the International Society for Peritoneal Dialysis. NMT discloses receipt of grants from the Collaborative Research Center 1192, European Research Council, and Else Kröner-Fresenius-Stiftung; receipt of consulting fees from Merida Biosciences; speaker honoraria from AstraZeneca, CSL Vifor, and Novartis; and ownership of patents 1878LU (pending) and EP2015/066881. MV discloses receipt of consulting fees from Novartis and Sobi; speaker honoraria from Alexion, Cambridge Medical, GSK, Novartis, Roche, Travere, Vifor Pharma, and WebMD; and serving as a renal expert for the European Society for Paediatric Nephrology connect4children (c4c) network. MEG discloses receipt of grants from the National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases, NIH/National Heart, Lung, and Blood Institute, and National Kidney Foundation; receipt of speaker honoraria from the Columbia University Medical Center, the Nephrology Self-Assessment Program of the American Society of Nephrology, and the University of Pennsylvania; travel support from the European Renal Association, the Hong Kong Society of Nephrology, KDIGO, the Kidney Research Institute, the Korean Society of Nephrology, and the University of Pennsylvania; and serving as volunteer Co-Chair of KDIGO and on boards or committees for the *American Journal of Kidney Diseases*, the American Society of Nephrology, the *Clinical Journal of the American Society of Nephrology*, the *Journal of the American Society of Nephrology*, the Kidney Institute, the National Kidney Foundation, and the United States Renal Data System. MJ discloses receipt of consulting fees from Astellas, AstraZeneca, Boehringer Ingelheim, Menarini, and STADA; receipt of speaker honoraria from Astellas, AstraZeneca, Boehringer Ingelheim, CSL Vifor, GSK, Novo Nordisk, STADA EG, and Vertex; receipt of travel support from AstraZeneca, Boehringer Ingelheim, and GSK; and serving as a volunteer Co-Chair of KDIGO and a volunteer co-president of the European Kidney Health Alliance. BHR discloses receipt of grants and travel support from Alexion, Aurinia Pharmaceuticals, AstraZeneca, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Calliditas Therapeutics, GSK, Lucin, the Lupus Foundation of America, NephroNet, NIH, Novartis, Otsuka, Roche-Genentech, Travere, and Vera Therapeutics; and participation on advisory boards for AstraZeneca, Aurinia Pharmaceuticals, Biogen Idec, and NephroNet. All the other authors declared no competing interests.

ACKNOWLEDGMENTS

The authors thank Tanya Green and Coral Cyzewski of Kidney Disease: Improving Global Outcomes (KDIGO) for assisting with conference planning and implementation and Debbie Maizels of Zoobotanica Scientific Illustration for assisting with figure illustrations.

FUNDING

The conference was sponsored by Kidney Disease: Improving Global Outcomes (KDIGO) and was in part supported by unrestricted educational grants from Alexion, Biogen, Cabaletta Bio, Calliditas Therapeutics, Incyte, Jade Biosciences, Novartis, Otsuka, Roche, Takeda, Trotana, Vera Therapeutics, and Vertex Pharmaceuticals.

REFERENCES

1. Rovin BH, Furie R, Latinis K, et al. Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: the Lupus Nephritis Assessment with Rituximab study. *Arthritis Rheumatol*. 2012;64:1215–1226.

2. Isaka Y, Sakaguchi Y, Shinzawa M, et al. Rituximab for relapsing nephrotic syndrome in adults: a randomized clinical trial. *JAMA*. 2025;334:2011–2019.
3. Furie RA, Rovin BH, Garg JP, et al. Efficacy and safety of obinutuzumab in active lupus nephritis. *N Engl J Med*. 2025;392:1471–1483.
4. Fervenza FC, Appel GB, Barbour SJ, et al. Rituximab or cyclosporine in the treatment of membranous nephropathy. *N Engl J Med*. 2019;381:36–46.
5. Stone JH, Merkel PA, Spiera R, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. *N Engl J Med*. 2010;363:221–232.
6. Perico L, Casiraghi F, Sònego F, et al. Bi-specific autoantigen-T cell engagers as targeted immunotherapy for autoreactive B cell depletion in autoimmune diseases. *Front Immunol*. 2024;15:1335998.
7. Albayrak G, Wan PK, Fisher K, et al. T cell engagers: expanding horizons in oncology and beyond. *Br J Cancer*. 2025;133:1241–1249.
8. Mougiakakos D, Meyer EH, Schett G. CAR T cells in autoimmunity: game changer or stepping stone? *Blood*. 2025;145:1841–1849.
9. Mei HE, Wirries I, Frölich D, et al. A unique population of IgG-expressing plasma cells lacking CD19 is enriched in human bone marrow. *Blood*. 2015;125:1739–1748.
10. Halliley JL, Tipton CM, Liesveld J, et al. Long-lived plasma cells are contained within the CD19⁺CD38^{hi}CD138⁺ subset in human bone marrow. *Immunity*. 2015;43:132–145.
11. Suan D, Moore J, Goodnow CC. Can autoimmune disease be cured by deep CD19⁺ cell depletion? *J Immunol*. 2025;214:1075–1092.
12. Cheung CK, Barratt J, Liew A, et al. The role of BAFF and APRIL in IgA nephropathy: pathogenic mechanisms and targeted therapies. *Front Nephrol*. 2023;3:1346769.
13. Stamellou E, Seikrit C, Tang SCW, et al. IgA nephropathy. *Nat Rev Dis Primers*. 2023;9:67.
14. Cheung CK, Alexander S, Reich HN, et al. The pathogenesis of IgA nephropathy and implications for treatment. *Nat Rev Nephrol*. 2025;21:9–23.
15. Haas M, Meehan SM, Karrison TG, et al. Changing etiologies of unexplained adult nephrotic syndrome: a comparison of renal biopsy findings from 1976–1979 and 1995–1997. *Am J Kidney Dis*. 1997;30:621–631.
16. Braden GL, Mulhern JG, O'Shea MH, et al. Changing incidence of glomerular diseases in adults. *Am J Kidney Dis*. 2000;35:878–883.
17. Beck LH Jr, Bonegio RG, Lambeau G, et al. M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. *N Engl J Med*. 2009;361:11–21.
18. Tomas NM, Beck LH Jr, Meyer-Schwesinger C, et al. Thrombospondin type-1 domain-containing 7A in idiopathic membranous nephropathy. *N Engl J Med*. 2014;371:2277–2287.
19. Colucci M, Carsetti R, Serafinelli J, et al. Prolonged impairment of immunological memory after anti-CD20 treatment in pediatric idiopathic nephrotic syndrome. *Front Immunol*. 2019;10:1653.
20. Tomas NM, Hoxha E, Reinicke AT, et al. Autoantibodies against thrombospondin type 1 domain-containing 7A induce membranous nephropathy. *J Clin Invest*. 2016;126:2519–2532.
21. Reinhard L, Wiech T, Reitmeier A, et al. Pathogenicity of human anti-PLA 2 R1 antibodies in minipigs: a pilot study. *J Am Soc Nephrol*. 2023;34:369–373.
22. Seifert L, Zahner G, Meyer-Schwesinger C, et al. The classical pathway triggers pathogenic complement activation in membranous nephropathy. *Nat Commun*. 2023;14:473.
23. Tomas NM, Dehde S, Meyer-Schwesinger C, et al. Podocyte expression of human phospholipase A2 receptor 1 causes immune-mediated membranous nephropathy in mice. *Kidney Int*. 2023;103:297–303.
24. Tomas NM, Schnarre A, Dehde S, et al. Introduction of a novel chimeric active immunization mouse model of PLA2R1-associated membranous nephropathy. *Kidney Int*. 2023;104:916–928.
25. Zahner G, Dehde S, Seifert L, et al. Patient anti-PLA2R1 autoantibodies cause membranous nephropathy in human PLA2R1 transgenic mice. *Kidney Int*. 2025;108:1179–1183.
26. Burbelo PD, Joshi M, Chaturvedi A, et al. Detection of PLA2R autoantibodies before the diagnosis of membranous nephropathy. *J Am Soc Nephrol*. 2020;31:208–217.
27. Hoxha E, Thiele I, Zahner G, et al. Phospholipase A2 receptor autoantibodies and clinical outcome in patients with primary membranous nephropathy. *J Am Soc Nephrol*. 2014;25:1357–1366.

28. Kanigicherla D, Gummada J, McKenzie EA, et al. Anti-PLA2R antibodies measured by ELISA predict long-term outcome in a prevalent population of patients with idiopathic membranous nephropathy. *Kidney Int.* 2013;83:940–948.
29. Hoxha E, Harendza S, Pinn Schmidt H, et al. M-type phospholipase A2 receptor autoantibodies and renal function in patients with primary membranous nephropathy. *Clin J Am Soc Nephrol.* 2014;9:1883–1890.
30. Bech AP, Hofstra JM, Brenchley PE, et al. Association of anti-PLA2R antibodies with outcomes after immunosuppressive therapy in idiopathic membranous nephropathy. *Clin J Am Soc Nephrol.* 2014;9:1386–1392.
31. Dahan K, Gillion V, Johanet C, et al. The role of PLA2R antibody in treatment of membranous nephropathy. *Kidney Int Rep.* 2018;3:498–501.
32. Xipell M, Rodas LM, Villarreal J, et al. The utility of phospholipase A2 receptor autoantibody in membranous nephropathy after kidney transplantation. *Clin Kidney J.* 2018;11:422–428.
33. Mahmud M, Pinn Schmidt HO, Reinhard L, et al. Role of phospholipase A2 receptor 1 antibody level at diagnosis for long-term renal outcome in membranous nephropathy. *PLoS One.* 2019;14:e0221293.
34. Navarro-Torres M, Wooden B, Santoriello D, et al. Podocytopathies. *Adv Kidney Dis Health.* 2025;32:2–11.
35. Watts AJB, Keller KH, Lerner G, et al. Discovery of autoantibodies targeting nephrin in minimal change disease supports a novel autoimmune etiology. *J Am Soc Nephrol.* 2022;33:238–252.
36. Shirai Y, Miura K, Ishizuka K, et al. A multi-institutional study found a possible role of anti-nephrin antibodies in post-transplant focal segmental glomerulosclerosis recurrence. *Kidney Int.* 2024;105:608–617.
37. Hengel FE, Dehde S, Lassé M, et al. Autoantibodies targeting nephrin in podocytopathies. *N Engl J Med.* 2024;391:422–433.
38. Hengel FE, Dehde S, Yilmaz A, et al. Anti-nephrin autoantibodies in steroid-resistant nephrotic syndrome may inform treatment strategy. *Kidney Int.* 2025;107:1099–1103.
39. Batal I, Watts AJB, Gibier JB, et al. Pre-transplant anti-nephrin antibodies are specific predictors of recurrent diffuse podocytopathy in the kidney allograft. *Kidney Int.* 2024;106:749–752.
40. Shu Y, Huang J, Jiang L, et al. Anti-nephrin antibodies in adult Chinese patients with minimal change disease and primary focal segmental glomerulosclerosis. *Kidney Int.* 2025;108:433–444.
41. Raglianti V, Angelotti ML, Cirillo L, et al. Anti-slit diaphragm antibodies on kidney biopsy identify pediatric patients with steroid-resistant nephrotic syndrome responsive to second-line immunosuppressants. *Kidney Int.* 2024;106:1124–1134.
42. Hengel FE, Dehde S, Kretz O, et al. Passive transfer of patient-derived anti-nephrin autoantibodies causes a podocytopathy with minimal change lesions. *J Clin Invest.* 2025;135:e186769.
43. Raglianti V, Angelotti ML, De Chiara L, et al. Anti-slit antibodies against podocin and Kirrel1 in pediatric and adult podocytopathies. *J Am Soc Nephrol.* 2025;36:702–705.
44. Fribourg M, Cioni M, Ghiggeri G, et al. CyTOF-enabled analysis identifies class-switched B cells as the main lymphocyte subset associated with disease relapse in children with idiopathic nephrotic syndrome. *Front Immunol.* 2021;12:726428.
45. Bhatia D, Sinha A, Hari P, et al. Rituximab modulates T- and B-lymphocyte subsets and urinary CD80 excretion in patients with steroid-dependent nephrotic syndrome. *Pediatr Res.* 2018;84:520–526.
46. Colucci M, Angeletti A, Zotta F, et al. Age and memory B cells at baseline are associated with risk of relapse and memory B-cell reappearance following anti-CD20 treatment in pediatric frequently-relapsing/steroid-dependent nephrotic syndrome. *Kidney Int.* 2023;104:577–586.
47. Colucci M, Carsetti R, Cascioli S, et al. B cell reconstitution after rituximab treatment in idiopathic nephrotic syndrome. *J Am Soc Nephrol.* 2016;27:1811–1822.
48. Parodis I, Rovin BH, Tektonidou MG, et al. Lupus nephritis. *Nat Rev Dis Primers.* 2025;11:69.
49. Arbuckle MR, McClain MT, Rubertone MV, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med.* 2003;349:1526–1533.
50. Furie R, Rovin BH, Houssiau F, et al. Two-year, randomized, controlled trial of belimumab in lupus nephritis. *N Engl J Med.* 2020;383:1117–1128.
51. Mathur M, Chan TM, Oh KH, et al. A Proliferation-Inducing Ligand (APRIL) in the pathogenesis of immunoglobulin A nephropathy: a review of the evidence. *J Clin Med.* 2023;12:6927.
52. Schrezenmeier E, Jayne D, Dörner T. Targeting B cells and plasma cells in glomerular diseases: translational perspectives. *J Am Soc Nephrol.* 2018;29:741–758.
53. Hunter TL, Bao Y, Zhang Y, et al. In vivo CAR T cell generation to treat cancer and autoimmune disease. *Science.* 2025;388:1311–1317.
54. Lafayette RA, Canetta PA, Rovin BH, et al. A randomized, controlled trial of rituximab in IgA nephropathy with proteinuria and renal dysfunction. *J Am Soc Nephrol.* 2017;28:1306–1313.
55. Hartono C, Chung M, Perlman AS, et al. Bortezomib for reduction of proteinuria in IgA nephropathy. *Kidney Int Rep.* 2018;3:861–866.
56. Floege J, Lafayette R, Barratt J, et al. Randomized, double-blind, placebo-controlled phase 2a study assessing the efficacy and safety of felzartamab for IgA nephropathy. *Kidney Int.* 2025;108:695–706.
57. Barratt J, Suzuki Y, Nguyen VA, et al. Safety, tolerability, and efficacy of mezagitamab (TAK-079) as add-on to standard of care therapy in individuals with primary IgA nephropathy: interim results from an open-label phase 1b study: FR-PO857. *J Am Soc Nephrol.* 2024;35:https://doi.org/10.1681/ASN.20243d24074tq
58. Mathur M, Barratt J, Chacko B, et al. A phase 2 trial of sibeprenlimab in patients with IgA nephropathy. *N Engl J Med.* 2024;390:20–31.
59. Perkovic V, Trimarchi H, Tesar V, et al. Sibeprenlimab in IgA nephropathy—interim analysis of a phase 3 trial. *N Engl J Med.* 2026;394:635–646.
60. Kooienga L, Lo J, Lee EY, et al. Zigakibart demonstrates clinical safety and efficacy in a phase 1/2 trial of healthy volunteers and patients with IgA nephropathy. *Kidney Int.* 2025;108:445–454.
61. Lafayette R, Barbour S, Israni R, et al. A phase 2b, randomized, double-blind, placebo-controlled, clinical trial of atacicept for treatment of IgA nephropathy. *Kidney Int.* 2024;105:1306–1315.
62. Barratt J, Barbour SJ, Brenner RM, et al. Long-term results from an open-label extension study of atacicept for the treatment of IgA nephropathy. *J Am Soc Nephrol.* 2025;36:679–687.
63. Lafayette R, Barbour SJ, Brenner RM, et al. A phase 3 trial of atacicept in patients with IgA nephropathy. *N Engl J Med.* 2026;394:647–657.
64. Lv J, Liu L, Hao C, et al. Randomized phase 2 trial of telitacept in patients with IgA nephropathy with persistent proteinuria. *Kidney Int Rep.* 2023;8:499–506.
65. Madan A, Yalavarthy R, Kim DK, et al. Results from longer follow-up with povetacept, an enhanced dual BAFF/APRIL antagonist, in IgA nephropathy (RUBY-3 study): FR-PO854. *J Am Soc Nephrol.* 2024;35:https://doi.org/10.1681/ASN.2024b1682rbd1636
66. Barratt J, Barbour S, Brenner R, et al. #2859 ORIGIN 2b: changes in Gd-IgA1 and eGFR after discontinuation of atacicept treatment in IgA nephropathy. *Nephrol Dial Transplant.* 2025;40(suppl 3):gaf116.0256.
67. Fervenza FC, Abraham RS, Erickson SB, et al. Rituximab therapy in idiopathic membranous nephropathy: a 2-year study. *Clin J Am Soc Nephrol.* 2010;5:2188–2198.
68. Beck LH Jr, Fervenza FC, Beck DM, et al. Rituximab-induced depletion of anti-PLA2R autoantibodies predicts response in membranous nephropathy. *J Am Soc Nephrol.* 2011;22:1543–1550.
69. Cravedi P, Sghirlanzoni MC, Marasa M, et al. Efficacy and safety of rituximab second-line therapy for membranous nephropathy: a prospective, matched-cohort study. *Am J Nephrol.* 2011;33:461–468.
70. Dahan K, Debiec H, Plaisier E, et al. Rituximab for severe membranous nephropathy: a 6-month trial with extended follow-up. *J Am Soc Nephrol.* 2017;28:348–358.
71. Dahan K, Johannet C, Esteve E, et al. Retreatment with rituximab for membranous nephropathy with persistently elevated titers of anti-phospholipase A2 receptor antibody. *Kidney Int.* 2019;95:233–234.
72. Fernandez-Juarez G, Rojas-Rivera J, Logt AV, et al. The STARMEN trial indicates that alternating treatment with corticosteroids and cyclophosphamide is superior to sequential treatment with tacrolimus and rituximab in primary membranous nephropathy. *Kidney Int.* 2021;99:986–998.
73. Scolari F, Delbarba E, Santoro D, et al. Rituximab or cyclophosphamide in the treatment of membranous nephropathy: the RI-CYCLO randomized trial. *J Am Soc Nephrol.* 2021;32:972–982.
74. Ramachandran R, Nayak S, Kumar V, et al. Rituximab in primary membranous nephropathy: a comparative study of three dosing regimens. *Nephrol Dial Transplant.* 2021;36:1352–1354.
75. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int.* 2021;100(4S):S1–S276.

76. Sethi S, Kumar S, Lim K, et al. Obinutuzumab is effective for the treatment of refractory membranous nephropathy. *Kidney Int Rep.* 2020;5:1515–1518.
77. Lin Y, Han Q, Chen L, et al. Obinutuzumab in refractory membranous nephropathy: a case series. *Kidney Med.* 2024;6:100853.
78. Teisseyre M, Allinovi M, Audard V, et al. Obinutuzumab and ofatumumab are more effective than rituximab in the treatment of membranous nephropathy patients with anti-rituximab antibodies. *Kidney Int Rep.* 2025;10:753–761.
79. Podestà MA, Trillini M, Portalupi V, et al. Ofatumumab in rituximab-resistant and rituximab-intolerant patients with primary membranous nephropathy: a case series. *Am J Kidney Dis.* 2024;83:340–349.e341.
80. Rovin BH, Ronco PM, Wetzels JFM, et al. Phase 1b/2a study assessing the safety and efficacy of felzartamab in anti-phospholipase A2 receptor autoantibody-positive primary membranous nephropathy. *Kidney Int Rep.* 2024;9:2635–2647.
81. Nachman PH, Stelzig L, Sherman MA, et al. Belimumab and rituximab for the treatment of primary membranous nephropathy: initial REBOOT results: TH-PO586. *J Am Soc Nephrol.* 2024;35. <https://doi.org/10.1681/ASN.20249xdwh001>
82. Madan A, Yalavarthy R, Kim DK, et al. AIS-D03 RUBY-3 Study Group. Poretacicept for IgA nephropathy and primary membranous nephropathy. *Kidney Int Rep.* 2025;11:106–116.
83. Ronco P, Beck L, Debiec H, et al. Membranous nephropathy. *Nat Rev Dis Primers.* 2021;7:69.
84. Podestà MA, Gennarini A, Portalupi V, et al. Accelerating the depletion of circulating anti-phospholipase A2 receptor antibodies in patients with severe membranous nephropathy: preliminary findings with double filtration plasmapheresis and ofatumumab. *Nephron.* 2020;144:30–35.
85. Müller F, Taubmann J, Bucci L, et al. CD19 CAR T-cell therapy in autoimmune disease—a case series with follow-up. *N Engl J Med.* 2024;390:687–700.
86. Muller F, Wirsching A, Hagen M, et al. BCMA CAR T cells in a patient with relapsing idiopathic inflammatory myositis after initial and repeat therapy with CD19 CAR T cells. *Nat Med.* 2025;31:1793–1797.
87. Mackensen A, Müller F, Mougiakakos D, et al. Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. *Nat Med.* 2022;28:2124–2132.
88. Marin D, Li Y, Basar R, et al. Safety, efficacy and determinants of response of allogeneic CD19-specific CAR-NK cells in CD19+ B cell tumors: a phase 1/2 trial. *Nat Med.* 2024;30:772–784.
89. Seifert L, Riecken K, Zahner G, et al. An antigen-specific chimeric autoantibody receptor (CAAR) NK cell strategy for the elimination of anti-PLA2R1 and anti-THSD7A antibody-secreting cells. *Kidney Int.* 2024;105:886–889.
90. Altun B, Zhao G, Wang B, et al. Preclinical evaluation of antigen-specific B-cell depletion for phospholipase A2 receptor membranous nephropathy with chimeric autoantibody receptor T cells. *Kidney Int.* 2026;109:89–100.
91. Larkins NG, Hahn D, Liu ID, et al. Non-corticosteroid immunosuppressive medications for steroid-sensitive nephrotic syndrome in children. *Cochrane Database Syst Rev.* 2024;11:CD002290.
92. Liu J, Deng F, Wang X, et al. Early rituximab as an add-on therapy in children with the initial episode of nephrotic syndrome. *Kidney Int Rep.* 2024;9:1220–1227.
93. Sheng AQ, Liu F, Li QY, et al. The efficacy and safety of rituximab monotherapy in the new onset pediatric idiopathic nephrotic syndrome: a randomized controlled clinical trial. *Ren Fail.* 2025;47:2499902.
94. Luo N, Shen X, Xia H, et al. Efficacy and safety of rituximab in children with steroid-dependent or frequently relapsing nephrotic syndrome: a meta-analysis of randomized controlled trials. *Arch Med Sci.* 2025;21:588–596.
95. Chan EY, Yap DY, Colucci M, et al. Use of rituximab in childhood idiopathic nephrotic syndrome. *Clin J Am Soc Nephrol.* 2023;18:533–548.
96. Iijima K, Sako M, Oba M, et al. Mycophenolate mofetil after rituximab for childhood-onset complicated frequently-relapsing or steroid-dependent nephrotic syndrome. *J Am Soc Nephrol.* 2022;33:401–419.
97. Zotta F, Vivarelli M, Emma F. Update on the treatment of steroid-sensitive nephrotic syndrome. *Pediatr Nephrol.* 2022;37:303–314.
98. Blanco E, Pérez-Andrés M, Arriba-Méndez S, et al. Age-associated distribution of normal B-cell and plasma cell subsets in peripheral blood. *J Allergy Clin Immunol.* 2018;141:2208–2219.e2216.
99. Ravani P, Colucci M, Bruschi M, et al. Human or chimeric monoclonal anti-CD20 antibodies for children with nephrotic syndrome: a superiority randomized trial. *J Am Soc Nephrol.* 2021;32:2652–2663.
100. Dossier C, Bonneric S, Baudouin V, et al. Obinutuzumab in frequently relapsing and steroid-dependent nephrotic syndrome in children. *Clin J Am Soc Nephrol.* 2023;18:1555–1562.
101. Feder O, Amsterdam D, Ershed M, et al. Long-term efficacy of rituximab in steroid dependent and frequent relapsing adult nephrotic syndrome. *BMC Nephrol.* 2025;26:126.
102. Lan L, Lin Y, Yu B, et al. Efficacy of rituximab for minimal change disease and focal segmental glomerulosclerosis with frequently relapsing or steroid-dependent nephrotic syndrome in adults: a Chinese multicenter retrospective study. *Am J Nephrol.* 2024;55:25–36.
103. Zhong H, Li HY, Zhou T, et al. Rituximab therapy in adults with steroid-dependent nephrotic syndrome. *Arch Med Sci.* 2023;19:577–585.
104. Iwabuchi Y, Takei T, Moriyama T, et al. Long-term prognosis of adult patients with steroid-dependent minimal change nephrotic syndrome following rituximab treatment. *Medicine.* 2014;93:e300.
105. Hoxha E, Stahl RA, Harendza S. Rituximab in adult patients with immunosuppressive-dependent minimal change disease. *Clin Nephrol.* 2011;76:151–158.
106. Guan N, Zhang M, Zhang M, et al. Rituximab as initial therapy in adult patients with minimal change disease. *Kidney Int Rep.* 2023;8:1102–1104.
107. Li X, Yan P, Zhang L, et al. The efficacy and safety of half-dose glucocorticoids combined with rituximab versus high-dose glucocorticoids for initial treatment of minimal change disease: a single-center experience. *Front Pharmacol.* 2024;15:1403562.
108. Vivarelli M, Colucci M, Gargiulo A, et al. Belimumab for the treatment of children with frequently relapsing nephrotic syndrome: the BELNEPH study. *Pediatr Nephrol.* 2022;37:377–383.
109. Angeletti A, Bin S, Kajana X, et al. Combined rituximab and daratumumab treatment in difficult-to-treat nephrotic syndrome cases. *Kidney Int Rep.* 2024;9:1892–1896.
110. Angeletti A, Bin S, Magnasco A, et al. Efficacy of combined rituximab and daratumumab treatment in posttransplant recurrent focal segmental glomerulosclerosis. *Am J Transplant.* 2024;24:688–692.
111. Delbet JD, Hogan J, Parmentier C, et al. Successful global anti-B-cell strategy with daratumumab in a patient with post-transplant nephrotic syndrome recurrence unresponsive to immunoadsorption and obinutuzumab. *Pediatr Transplant.* 2023;27:e14544.
112. Dossier C, Hogan J. Reply to Angeletti et al—efficacy of combined rituximab and daratumumab treatment in posttransplant recurrent focal segmental glomerulosclerosis. *Am J Transplant.* 2024;24:1325–1326.
113. Mysler EF, Spindler AJ, Guzman R, et al. Efficacy and safety of ocrelizumab in active proliferative lupus nephritis: results from a randomized, double-blind, phase III study. *Arthritis Rheumatol.* 2013;65:2368–2379.
114. Furie RA, Aroca G, Cascino MD, et al. B-cell depletion with obinutuzumab for the treatment of proliferative lupus nephritis: a randomised, double-blind, placebo-controlled trial. *Ann Rheum Dis.* 2022;81:100–107.
115. Gomez Mendez LM, Cascino MD, Garg J, et al. Peripheral blood B cell depletion after rituximab and complete response in lupus nephritis. *Clin J Am Soc Nephrol.* 2018;13:1502–1509.
116. Looney CM, Schroeder A, Tavares E, et al. Obinutuzumab effectively depletes key B-cell subsets in blood and tissue in end-stage renal disease patients. *Transplant Direct.* 2023;9:e1436.
117. Rovin B, Alberton VG, Gonçalves Martins E, et al. Beyond clinical response in the REGENCY trial: the impact of obinutuzumab on histologic remission in patients with active lupus nephritis: SA-OR084. *J Am Soc Nephrol.* 2025;36. <https://doi.org/10.1681/ASN.2025ap1689ae1681n1681>
118. Tobinai K, Klein C, Oya N, et al. A review of obinutuzumab (GA101), a novel type II anti-CD20 monoclonal antibody, for the treatment of patients with B-cell malignancies. *Adv Ther.* 2017;34:324–356.
119. Kidney Disease: Improving Global Outcomes (KDIGO) Lupus Nephritis Work Group. KDIGO 2024 Clinical Practice Guideline for the Management of Lupus Nephritis. *Kidney Int.* 2024;105(1S):S1–S69.
120. Sammaritano LR, Askanase A, Bermas BL, et al. 2024 American College of Rheumatology (ACR) Guideline for the Screening, Treatment, and Management of Lupus Nephritis. *Arthritis Rheumatol.* 2025;77:1115–1135.
121. Fanouriakis A, Kostopoulou M, Anders HJ, et al. EULAR recommendations for the management of systemic lupus erythematosus with kidney involvement: 2025 update. *Ann Rheum Dis.* 2026;85:75–90.
122. Segarra A, Arredondo KV, Jaramillo J, et al. Efficacy and safety of bortezomib in refractory lupus nephritis: a single-center experience. *Lupus.* 2020;29:118–125.

123. Ostendorf L, Burns M, Durek P, et al. Targeting CD38 with daratumumab in refractory systemic lupus erythematosus. *N Engl J Med*. 2020;383:1149–1155.
124. Roccatello D, Fenoglio R, Caniggia I, et al. Daratumumab monotherapy for refractory lupus nephritis. *Nat Med*. 2023;29:2041–2047.
125. Wang W, He S, Zhang W, et al. BCMA-CD19 compound CAR T cells for systemic lupus erythematosus: a phase 1 open-label clinical trial. *Ann Rheum Dis*. 2024;83:1304–1314.
126. Schett G, Nagy G, Krönke G, et al. B-cell depletion in autoimmune diseases. *Ann Rheum Dis*. 2024;83:1409–1420.
127. Tur C, Eckstein M, Velden J, et al. CD19-CAR T-cell therapy induces deep tissue depletion of B cells. *Ann Rheum Dis*. 2025;84:106–114.
128. Delestre F, Charles P, Karras A, et al. Rituximab as maintenance therapy for ANCA-associated vasculitides: pooled analysis and long-term outcome of 277 patients included in the MAINRITSAN trials. *Ann Rheum Dis*. 2024;83:233–241.
129. Amudala NA, Boukhalil S, Sheridan B, et al. Obinutuzumab as treatment for ANCA-associated vasculitis. *Rheumatology*. 2022;61:3814–3817.
130. Jayne D, Blockmans D, Luqmani R, et al. Efficacy and safety of belimumab and azathioprine for maintenance of remission in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized controlled study. *Arthritis Rheumatol*. 2019;71:952–963.
131. Schultze-Florey CR, Gödecke V, Knoll L, et al. Point-of-care anti-CD19-CAR T-cell therapy induces renal remission in refractory myeloperoxidase-antineutrophil cytoplasmic autoantibody-associated vasculitis. *Kidney Int Rep*. 2025;10:2491–2493.
132. Minopoulou I, Wilhelm A, Albach F, et al. Anti-CD19 CAR T cell therapy induces antibody seroconversion and complete B cell depletion in the bone marrow of a therapy-refractory patient with ANCA-associated vasculitis. *Ann Rheum Dis*. 2025;84:e4–e7.
133. Haghighi A, Hegelmaier T, Wolleschak D, et al. Clinical efficacy and autoantibody seroconversion with CD19-CAR T cell therapy in a patient with rheumatoid arthritis and coexisting myasthenia gravis. *Ann Rheum Dis*. 2024;83:1597–1598.
134. Berthou F, Suzuki H, Thibaudin L, et al. Autoantibodies targeting galactose-deficient IgA1 associate with progression of IgA nephropathy. *J Am Soc Nephrol*. 2012;23:1579–1587.
135. Dotz V, Visconti A, Lomax-Browne HJ, et al. O- and N-Glycosylation of serum immunoglobulin A is associated with IgA nephropathy and glomerular function. *J Am Soc Nephrol*. 2021;32:2455–2465.
136. Pei G, Zeng R, Han M, et al. Renal interstitial infiltration and tertiary lymphoid organ neogenesis in IgA nephropathy. *Clin J Am Soc Nephrol*. 2014;9:255–264.
137. Popova A, Slisere B, Racenis K, et al. IgA class-switched CD27–CD21+ B cells in IgA nephropathy. *Nephrol Dial Transplant*. 2025;40:505–515.
138. Hoxha E, Beck LH Jr, Wiech T, et al. An indirect immunofluorescence method facilitates detection of thrombospondin type 1 domain-containing 7A-specific antibodies in membranous nephropathy. *J Am Soc Nephrol*. 2017;28:520–531.
139. Wang H, Lan L, Wang J, et al. Alterations of B-cell subsets in peripheral blood from adult patients with idiopathic membranous nephropathy. *Immunol Lett*. 2024;266:106838.
140. Colucci M, Carsetti R, Cascioli S, et al. B cell phenotype in pediatric idiopathic nephrotic syndrome. *Pediatr Nephrol*. 2019;34:177–181.
141. Ling C, Wang X, Chen Z, et al. Altered B-lymphocyte homeostasis in idiopathic nephrotic syndrome. *Front Pediatr*. 2019;7:377.
142. Shao XS, Yang XQ, Zhao XD, et al. The prevalence of Th17 cells and FOXP3 regulate T cells (Treg) in children with primary nephrotic syndrome. *Pediatr Nephrol*. 2009;24:1683–1690.
143. Riganati M, Zotta F, Candino A, et al. A novel flow cytometry panel to identify prognostic markers for steroid-sensitive forms of idiopathic nephrotic syndrome in childhood. *Front Immunol*. 2024;15:1379924.
144. Casiraghi F, Todeschini M, Podestà MA, et al. Immunophenotypic alterations in adult patients with steroid-dependent and frequently relapsing nephrotic syndrome. *Int J Mol Sci*. 2023;24:7687.
145. Oniszczuk J, Beldi-Ferchiou A, Audureau E, et al. Circulating plasmablasts and high level of BAFF are hallmarks of minimal change nephrotic syndrome in adults. *Nephrol Dial Transplant*. 2021;36:609–617.
146. Al-Aubodah TA, Aoudjit L, Pascale G, et al. The extrafollicular B cell response is a hallmark of childhood idiopathic nephrotic syndrome. *Nat Commun*. 2023;14:7682.
147. Hengel FE, Huber TB, Tomas NM. Potential and pitfalls of measuring circulating anti-nephrin autoantibodies in glomerular diseases. *Clin Kidney J*. 2025;18:sfa100.
148. Mirioglu S, Bruchfeld A, Caravaca-Fontan F, et al. Quo vadis standardization of anti-nephrin antibody detection? *Glomerular Dis*. 2025;5:200–205.
149. Liu P, Liu S, Dalal V, et al. Evaluation of methodologies in anti-nephrin autoantibody detection. *Kidney Int*. 2025;108:485–490.
150. Habbig S, Debiec H, Chedik M, et al. Anti-nephrin antibodies guide living donor kidney transplantation in a pediatric patient with primary focal segmental glomerular sclerosis. *Kidney Int*. 2025;108:321–327.
151. Dall'Era M, Stone D, Levesque V, et al. Identification of biomarkers that predict response to treatment of lupus nephritis with mycophenolate mofetil or pulse cyclophosphamide. *Arthritis Care Res (Hoboken)*. 2011;63:351–357.
152. Specks U, Merkel PA, Seo P, et al. Efficacy of remission-induction regimens for ANCA-associated vasculitis. *N Engl J Med*. 2013;369:417–427.
153. Terrier B, Pagnoux C, Perrodeau É, et al. Long-term efficacy of remission-maintenance regimens for ANCA-associated vasculitides. *Ann Rheum Dis*. 2018;77:1150–1156.
154. Casal Moura M, Specks U, Tehranian S, et al. Maintenance of remission and risk of relapse in myeloperoxidase-positive ANCA-associated vasculitis with kidney involvement. *Clin J Am Soc Nephrol*. 2023;18:47–59.
155. Pagnoux C, Hogan SL, Chin H, et al. Predictors of treatment resistance and relapse in antineutrophil cytoplasmic antibody-associated small-vessel vasculitis: comparison of two independent cohorts. *Arthritis Rheumatol*. 2008;58:2908–2918.
156. Ramirez SI, Faraji F, Hills LB, et al. Immunological memory diversity in the human upper airway. *Nature*. 2024;632:630–636.
157. Hale M, Rawlings DJ, Jackson SW. The long and the short of it: insights into the cellular source of autoantibodies as revealed by B cell depletion therapy. *Curr Opin Immunol*. 2018;55:81–88.
158. Han S, Zhuang H, Shumyak S, et al. Mechanisms of autoantibody production in systemic lupus erythematosus. *Front Immunol*. 2015;6:228.
159. Liu Z, Zou Y, Davidson A. Plasma cells in systemic lupus erythematosus: the long and short of it all. *Eur J Immunol*. 2011;41:588–591.
160. Sinha A, Bhatia D, Gulati A, et al. Efficacy and safety of rituximab in children with difficult-to-treat nephrotic syndrome. *Nephrol Dial Transplant*. 2015;30:96–106.
161. Chan EY, Webb H, Yu E, et al. Both the rituximab dose and maintenance immunosuppression in steroid-dependent/frequently-relapsing nephrotic syndrome have important effects on outcomes. *Kidney Int*. 2020;97:393–401.
162. Zurowska A, Drozyska-Duklas M, Topaloglu R, et al. Rituximab-associated hypogammaglobulinemia in children with idiopathic nephrotic syndrome: results of an ESPN survey. *Pediatr Nephrol*. 2023;38:3035–3042.
163. Bonanni A, Calatroni M, D'Alessandro M, et al. Adverse events linked with the use of chimeric and humanized anti-CD20 antibodies in children with idiopathic nephrotic syndrome. *Br J Clin Pharmacol*. 2018;84:1238–1249.
164. Kamei K, Miyairi I, Ishikura K, et al. Prospective study of live attenuated vaccines for patients with nephrotic syndrome receiving immunosuppressive agents. *J Pediatr*. 2018;196:217–222.e211.
165. Chan EY, Yu ELM, Angeletti A, et al. Long-term efficacy and safety of repeated rituximab to maintain remission in idiopathic childhood nephrotic syndrome: an international study. *J Am Soc Nephrol*. 2022;33:1193–1207.
166. Adkins S. CAR T-cell therapy: adverse events and management. *J Adv Pract Oncol*. 2019;10:21–28.
167. Ellithi M, Elsallab M, Lunning MA, et al. Neurotoxicity and rare adverse events in BCMA-directed CAR T cell therapy: a comprehensive analysis of real-world FAERS data. *Transplant Cell Ther*. 2025;31:71.e1–71.e14.
168. Graham CE, Velasco R, Alarcon Tomas A, et al. Non-ICANS neurological complications after CAR T-cell therapies: recommendations from the EBMT Practice Harmonisation and Guidelines Committee. *Lancet Oncol*. 2025;26:e203–e213.
169. Mucha SR, Rajendram P. Management and prevention of cellular-therapy-related toxicity: early and late complications. *Curr Oncol*. 2023;30:5003–5023.