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Monitoring rituximab levels in primary membranous nephropathy; is it necessary for finding the perfect dose for lasting remission

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ABSTRACT

Primary membranous nephropathy (pMN) is characterized by thickening of the glomerular capillary wall and a variable course of disease. Rituximab, an anti-CD20 monoclonal antibody (mAb), has been shown to have therapeutic effects; however, optimal dosing regimens and monitoring practices remain uncertain. To assess the usefulness of rituximab level monitoring in pMN and determine the factors associated with variations in treatment effects. A literature review was conducted on studies comparing rituximab pharmacokinetics, monitoring methods, and clinical outcomes in pMN. Information on drug clearance, urinary loss, inactivation by antibodies, and Fc receptor polymorphisms were reviewed. Our review showed, ELISA is the most commonly employed method for rituximab quantification. However, uncertainty remains due to the large inter-patient variability. Drug availability is affected by urinary loss, internalization by B cells, anti-drug antibodies, and Fc receptor polymorphisms. Regular monitoring has been shown to reduce under- and over-treatment, favoring individualized therapies. Therefore, monitoring rituximab levels may facilitate precision-based treatment in pMN. Additionally, standardized protocols are needed for directing dosing, maintenance, and monitoring practices.

Review

Implication for health policy/practice/research/medical education:
Serial rituximab level monitoring in primary membranous nephropathy can facilitate precision-based, individualized treatment by detecting patients at risk for sub-therapeutic drug exposure due to phenomena such as urinary drug loss, anti-drug antibodies, or Fc receptor polymorphisms. The integration of standardized monitoring protocols for rituximab into clinical guidelines can minimize the risk of under- or over-treatment, maximize resource utilization, and enhance patient outcomes. Subsequent research and medical education should aim to confirm monitoring strategies in patient subgroups, incorporate pharmacokinetic evaluation into the practice of multiple disciplines, and establish evidence-based dosing algorithms for rituximab in patients with primary membranous nephropathy.

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Introduction

A specific pathological condition that affects the renal glomeruli and thickens the glomerular capillary walls is membranous nephropathy (MN). Immunological complexes on the outer aspect of the glomerular basement membrane are responsible for this thickening, and the resulting immunological activity leads to proteinuria, primarily driven by the pathophysiological disruption of podocyte structure caused by immune complex deposition and the formation of the membrane attack complex. Membranous nephropathy is responsible for approximately 30% of adult cases of nephrotic syndrome,

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of which 20% have secondary membranous nephropathy (sMN), which is associated with a particular etiology, while approximately 80% have primary membranous nephropathy (pMN) (1,2).

Over the past two decades, significant advancements have been made in the understanding of the pathogenesis of pMN. Autoantibodies targeting podocytes have long been suspected to cause human MN and its experimental counterpart, Heymann's nephritis. This hypothesis was supported in 1995 with the discovery of megalin as an autoantigen in Heymann nephritis. Rat podocytes and the luminal membrane of proximal tubule cells express megalin that plays a role in protein uptake. However, as megalin is only weakly expressed on human podocytes and is predominantly localized to the brush border of proximal tubules, it is unlikely to be the target antigen in human MN (3,4). In 2002, neutral endopeptidase (NEP) was identified as a relevant antigen in neonatal MN, where mothers with defective MME genes developed antibodies against fetal NEP during pregnancy. These antibodies cross the placenta and cause transient MN in newborns; NEP is normally expressed by podocytes (1,2,5). Since its discovery in 2009, the most significant autoantibody implicated in pMN targets the podocyte protein M-type "phospholipase A2 receptor 1" (PLA2R1) (2). Additional minor podocyte antigens identified since 2009 include "neural cell adhesion molecule-1" (NCAM-1), "exostosin-1 and exostosin-2" (EXT-1 and EXT-2), "neural epidermal growth factor-like 1" protein (NELL-1), "semaphorin 3B", "protocadherin 7" (PCDH7), "high-temperature requirement A serine peptidase 1" (HTRA1), and among others (6). Given the heterogeneous clinical course of MN, it is inappropriate to treat all patients similarly. Approximately one-half of the patients experience spontaneous remission without treatment, while the other half experience progressive deterioration of renal function. In addition to renal outcomes, comorbidities such as cardiovascular events and venous thromboembolism significantly affect morbidness and mortality in patients with MN and must be considered in their management (7). It is recommended that all patients with MN begin maximal conservative therapy, independent of immunosuppressive treatment. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines endorse conservative treatment for individuals with MN and proteinuria, including Angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARBs), diuretics, and sodium restriction to all ease edema and prevent cardiovascular events. The guidelines also recommend immunosuppression with rituximab alone or cyclophosphamide alternating months with glucocorticoid therapy (modified Ponticelli regimen) or calcineurin inhibitor therapy (8). While cyclophosphamide was originally prescribed to suppress the production of B cell antibody, the principal driver of disease activity, it is associated with a range of adverse effects (9).

Rituximab is a monoclonal antibody (mAb), formed with human and murine components. The CD20 transmembrane protein, found in B cells, is a specific target of rituximab (10). At present, the standard dose of rituximab given in guidelines is 1 g intravenous (IV) administered within two weeks or rituximab 375 mg/m^2 administered one to four times at weekly intervals. The quality of evidence for rituximab treatment remains low to moderate (11). According to a literature review, remission rates with rituximab varied widely, ranging from 20% to 70%, depending on the dosing regimen used. Due to the absence of a standardized dose and the influence of factors such as urinary excretion on rituximab clearance, no consensus guidelines exist for monitoring rituximab levels to inform treatment decisions. This review summarizes the pharmacokinetics of rituximab, analyzes studies employing various dosing protocols and their clinical outcomes, discusses factors contributing to rituximab underdosing, reviews available methods for measuring rituximab levels, and emphasizes the need for optimized dosing strategies in membranous nephropathy.

Methods

This review aims to consolidate the current knowledge regarding the monitoring of rituximab therapy in individuals with pMN. To achieve this, we conducted a comprehensive literature search using PubMed and Embase to identify relevant studies published between January 2000 and March 2025. A broad search strategy was employed, using combinations of keywords such as "rituximab" and "membranous nephropathy." Clinical trials, observational studies, and guidelines focusing on monitoring approaches in this context were included. Studies involving children, secondary causes of membranous nephropathy, and other study designs were excluded. Given the heterogeneity in study designs and outcomes, we provide a qualitative summary highlighting both common practices and variations in the monitoring approaches reported in the literature.

Pharmacokinetics of rituximab

The pharmacokinetics of rituximab in patients with MN vary according to the disease activity and severity. Significant alterations in pharmacokinetic properties have been observed during periods of marked, non-selective proteinuria. Variations in the reported pharmacokinetic parameters across studies are attributed to differences in disease types, pharmacokinetic mockups, and analytical approaches used (12). Bensalem et al employed a

consistent approach using concentration-time data from five studies to assess rituximab pharmacokinetics. However, substantial differences in pharmacokinetic characteristics between autoimmune and hematological diseases have been noted (13). The pharmacokinetics of rituximab and other mAbs are best described by a two-compartment model, in which elimination occurs either in the peripheral tissue compartment or the central plasma compartment. In autoimmune ailments, rituximab typically has a stable half-life, whereas in hematological diseases, its half-life usually extends during treatment as the number of excess target cells decreases (14). Notably, the severity of proteinuria significantly influences rituximab serum levels, resulting in a pharmacokinetic profile in nephrotic syndrome patients that is distinct from those with other indications. Serum rituximab concentrations in patients with MN are markedly lower than those in patients without proteinuria, such as individuals with myasthenia gravis or rheumatoid arthritis. Interestingly, retreatments were associated with higher rituximab concentrations, possibly indicating an improvement in nephrotic syndrome (15).

Absorption

Intravenous administration of rituximab results in 100% bioavailability, whereas subcutaneous (SC) administration only absorbs a fraction of the dose (60 %) due to proteolytic degradation or phagocytosis (16). Considering that the initial dose of rituximab has been reported to be more likely to cause infusion-related reactions, it is recommended to provide it intravenously so that it can be discontinued immediately if needed (12).

Distribution

After IV rituximab treatment, this drug attaches to the CD20 antigen on the external surface of viable or cancerous B cells in the peripheral bloodstream, bone marrow, and lymph nodes (16). Since rituximab does not cross the blood-brain barrier, it differs from other antibodies. In males with lymphoma, rheumatoid arthritis, and ANCA-associated vasculitis, the rituximab volume of distribution was significantly greater. One study found a favorable correlation between BSA and the volume of dispersal and clearance, both for subcutaneous and IV, in individuals with steroid-dependent and often relapsing nephrotic syndrome when children were included. FcRn greatly enhances immunoglobulin dispersion across tissues and promotes antibody circulation by lowering mAb degradation and facilitating mAb transport across endothelial cells. When everything is stable, the distribution volume of rituximab is approximately 9.6 L. With the central nervous system excluded, the 3–3.5 L plasma volume demonstrates that mAb diffuses throughout the extracellular spaces of the body parts (12). Research suggests that neonatal Fc receptor (FcRn) facilitates antibody outflow through the cerebrospinal fluid matrix rather than input into the central nervous system, while its exact role in bidirectional transport remains unclear (17).

Elimination

Internalization generated by a nonlinear, saturable, specific target and linear, nonspecific clearance mediated by both independent and FcγR-dependent pathways add up to the total clearance. Because FcRn recycles the antibody to the outward surface and releases it in the cell environment, binding to it usually results in a decrease in clearance. The interaction between mAbs and FcRn inhibits intracellular degradation. Total clearance (CL) sharply declines, and the elimination half-life lengthens with increasing rituximab concentrations as soon as the target-mediated elimination pathway hits saturation and approaches the linear process (CL_L) (17,18).

A significant amount of the difference in rituximab's efficacy in MN can be attributed to the pharmacokinetic alterations (13). In contrast to other autoimmune or hematologic disorders, rituximab has a shorter half-life with MN treatment (approximately 11.5 days), despite its negative correlation with urine protein excretion (19). Patients with MN-persuasive proteinuria had lower rituximab levels than those with non-proteinuric RA, according to Fervenza et al (20). Pharmacokinetic variables affect the efficacy of rituximab in B-cell non-Hodgkin's lymphoma; serum rituximab concentrations are considerably higher in responders than in non-responders. However, the cause of this inter-individual pharmacokinetic variability remains unknown. Reports have shown an inverse relationship between serum rituximab concentrations and pre-treatment tumor bulk and circulating B-lymphocyte levels. Therefore, pharmacokinetic studies are necessary to identify individual variability and investigate the link between rituximab concentration and effect (21).

Rituximab and its dosing in membranous nephropathy

Going back to rituximab's history, it was shown that even before the primary function of anti-phospholipase A2 receptor 1 (PLA2R) autoantibodies in the pathophysiology of MN was identified, antibodies produced from auto-reactive B cell clones were the cause of podocyte-related injury, glomerular filtration barrier impairment, and proteinuria (22).

By attaching itself to CD20, rituximab, a hybrid monoclonal IgG1 antibody, destroys B cells. Rituximab has been authorized by the US Food and Drug Administration and the European Medicines Agency to treat non-Hodgkin lymphoma, rheumatoid arthritis,

and anti-neutrophil cytoplasmic autoantibody-associated vasculitis (7). Although this medication is cleared through urine, rituximab bioavailability is decreased in patients with nephrotic syndrome. The rituximab dosing strategy for nephrotic patients remains debatable. As a second first-line therapy option, the KDIGO guidelines on glomerular disorders recommend either two applications of a fixed dose of 1 g within two weeks or 375 mg/m^2 administered one to four times at weekly intervals (8). The studies which used rituximab in pMN are summarized in Table 1.

Need for monitoring rituximab levels

Underdosing of rituximab is not unusual in pMN. Rituximab bioavailability is suggestively reduced in pMN linked to other autoimmune diseases without nephrotic syndrome due to its albumin-binding and loss in urine (35). Patients with pMN exhibit lower serum rituximab levels during follow-up than individuals without renal disease, likely because nephrotic syndrome causes rituximab to be lost through urine (7,19). This has therapeutic implications, as resistance to rituximab, vigorous disease, and early B lymphocyte recovery have been associated with undetectable drug levels at three months (36). For patients with PLA2R-associated MN, immunological monitoring appears to be a promising approach for guiding rituximab therapy (7,37).

Factors contributing to rituximab underdosing in pMN

Excretion of rituximab in urine

Severe proteinuria can cause irreversible and permanent damage to the glomerular filtration barrier. It can be difficult to differentiate between patients with secondary chronic irreversible glomerular damage and those resistant to several immunosuppressive medications (35). Stahl et al asserted that the degree of discrimination loss in the glomerular filter is the primary factor influencing the amount of rituximab lost in the urine (12,38). Analysis of IgG excretion in all collected samples revealed considerable levels of IgG in the urine of each patient. The ratios of IgG to creatinine and rituximab to creatinine showed a strong correlation when normalized to creatinine concentration, indicating that rituximab is excreted in the urine alongside increased IgG. Notably, in the first patient, proteinuria was higher before the initial rituximab dose and fluctuated over time, accompanied by a progressive increase in urinary rituximab excretion. Despite a significantly reduced serum half-life of less than one day and spaced rituximab doses over several weeks, the cumulative loss of glomerular selectivity may explain the patient's intermittent rise in urinary IgG excretion (15,38). The second case suggests that rituximab may be lost not only in the urine but also at a third site, potentially reducing its efficacy (38,39).

Anti-rituximab antibodies

Rituximab is a chimeric mAb composed of human IgG1 constant regions and murine anti-human CD20 variable regions (40). The formation of anti-drug antibodies (ADAs), such as anti-rituximab antibodies, complicates the use of chimeric mAbs. The development of ADAs significantly affects rituximab pharmacokinetics by increasing clearance (CL) by approximately 15%. Consequently, patients exhibiting shorter-than-expected rituximab half-lives and faster clearance rates may be suspected to have ADA development. Since ADAs can alter rituximab pharmacokinetics before they are detectable, patients should be evaluated for ADA presence after discontinuing rituximab therapy. ADAs may neutralize rituximab efficacy by binding to its variable domain, preventing antigen binding. Owing to their unpredictable formation, patients with anti- rituximab ADAs require continuous monitoring (41). If treatment fails, switching to alternative therapies containing different anti-CD20 molecules should be considered (28,41). Multiple factors contribute to ADA development, including age, sex, genetic profile, disease type, B cell count, rituximab formulation, and number of infusions (42). Among patients with pMN treated with rituximab, 23% to 43% develop anti-rituximab antibodies, which may be associated with a higher risk of relapse (38). For example, four rituximab-resistant patients with detectable anti-rituximab antibodies achieved remission only after treatment with obinutuzumab or ofatumumab. Conversely, four patients responded well to rituximab treatment without producing detectable anti-rituximab antibodies (43). Anti-rituximab antibodies were detected using ELISA, with a detection limit of 5 ng/mL established by the assay manufacturer (20).

B cell-mediated rituximab internalization and FcRn influence on therapy

Proximal tubule cells, glomerular podocytes, and endothelial cells are among the various tissues, vascular structures, and renal sites that express FcRn. The FcRn plays a critical role in the nonspecific elimination of therapeutic antibody. FcRn binds to distinct sites on IgG antibodies, extending their half-life to 7–21 days, and albumin, which has a half-life of approximately 21 days. The increased clearance of rituximab observed in patients with MN may result from mechanisms such as reduced therapeutic antibody binding affinity, decreased FcRn activity, or impaired FcRn function due to genetic polymorphisms in the FCGRT gene, as FcRn is pivotal in regulating IgG half-life (13,44). Important factors contributing to rituximab underdosing in pMN are summarized in Figure 1.

Table 1. Summary of the studies that used rituximab in primary membranous nephropathy

Author/year	Study design	Drug and dosage	Remission levels	Serum RTX/anti-rituximab antibodies measured
Chen et al, 2023 (23)	Retrospective cohort study	RTX 1g twice every two weeks; oral TAC: 0.03 mg/kg/d orally	Overall, RTX + TAC was 87.14% successful in treating refractory IMN, with 37.13% and 50.01% partial and complete remission rates, respectively.	NA
Destere et al, 2023 (24)	Machine learning algorithm	Eighty-four treatments consisted of two infusions of 1000 mg each, while eight treatments involved two infusions at a dose of 375 mg/m² each.	NA	Yes. When 92 rituximab levels were tested in these individuals three months after beginning rituximab treatment, 59.8% had levels below 2 µg/mL.
Ou et al, 2022 (25)	Systematic review		RTX improves remission, reduces relapses, and reduces antiphospholipase A2 antibody levels. First-line rituximab therapy showed a better remission rate than second-line therapy.	NA
Gao et al, 2021 (26)	Retrospective review	The initial dosage of rituximab (375 mg/m²) was administered four times a week.	In this study, 58.2% patients achieved clinical remission within twelve months.	NA
Teisseyre et al, 2021 (27)	Prospective cohort	RTX two infusions, 1 g infusions two weeks apart.	At six months, 53% of patients achieved clinical remission. By month twelve, 60% patients achieved clinical remission.	Yes. 44% of patients had blood rituximab levels above the threshold at three months. • 56% had undetectable levels. • There is a higher chance of clinical remission in patients whose blood rituximab levels are > 2 µg/mL at months 3 and 12. • Statistically significant difference observed at months 6 and 12.
Boyer-Suavet et al, 2019 (28)	Drug minimal cytotoxic concentration assessment	Two 1 g RTX injections were administered two weeks apart.	Remission was achieved in 79% of the patients after rituximab therapy.	Yes. Ten patients (23 percent) had anti-rituximab antibodies.
Scolari et al, 2021(29)	RCT	On days 1 and 15, 1 g RTX was administered. Cyclophosphamide: administer corticosteroids every other month.	Complete remission at 12 months: rituximab, 16% cyclophosphamide 32%. At 24 months, rituximab 62%, cyclophosphamide 73%.	NA
Fervenza et al, 2019 (20)	RCT	Two 1000 mg RTX infusions spaced two weeks apart are administered again at six months if there is partial remission. Cyclosporine: 3.5 mg daily for 12 months as an initial dose per kilogram of body weight.	Sixty % of the rituximab group and 52% of the cyclosporine group attained CR or PR at 12 months. At 24 months, the cyclosporine group and RTX group showed 20% and 60% remission, respectively.	NA
Seitz-Polski et al, 2019 (30)	RCT	RTX of two infusions at two-week interval.	At 6 months, in the NICE group 64%, while only 30% in the GEMRITUX cohort.	Yes At month three, residual rituximab levels were identified in 18 of the 28 patients in the NICE cohort, but only one of the 27 participants in the GEMRITUX group had detectable levels. The NICE cohort (3.3 mg/ml) had a higher retention than the GEMRITUX cohort (0.0 mg/ml), indicating a more successful retention of the medication in the NICE trial.

Table 1. Continued

Author/year	Study design	Drug and dosage	Remission levels	Serum RTX/anti-rituximab antibodies measured
Aleš Rigler et al, 2017 (31)	Retrospective analysis	375 mg/m^2 in 3-4 weekly doses	The remission rate after rituximab is 37.9%, and the highest remission rate is in patients with less than 4 g/day of proteinuria.	NA
Appel, 2012 (32)	Small pilot studies		In this study, 27% of patients achieved complete clinical remission. 38% of patients achieved partial remission.	NA
Dahan et al, 2017 (33)	RCT	RTX: 375 mg/m^2 given two intravenous infusions	Thirty-five percent of patients in the NIAT-rituximab group and twenty-one percent of patients in the NIAT group experienced remission at six months.	NA
Ruggenenti et al, 2003 (34)	Prospective observational study	RTX dosage: 375 mg/m^2 given four weekly infusions	RTX reduces proteinuria in idiopathic membranous nephropathy patients significantly and is also safe and promotes sustained disease remission.	NA

Abbreviations: RTX, Rituximab; TAC, Tacrolimus; NIAT, No immunosuppressive antiproteinuric treatment; RCT, Randomized controlled trial

Measurement of rituximab levels

Enzyme-linked immunosorbent assay (ELISA)

Serum rituximab levels vary widely among individuals who receive standard doses. Most ELISAs utilize polyclonal antibodies to capture rituximab and monoclonal antibodies for its detection. The ELISA demonstrated acceptable sensitivity, with a dynamic range of 3–80 ng/mL, as determined by spiking tests. This range indicates that the assay can accurately detect low quantities of rituximab in serum samples, which is essential for pharmacokinetic studies. The assay precision was evaluated, revealing a within-day precision (coefficient of variation; CV) of less than 10% and a between-day precision CV of less than 25%, indicating reliable quantification of rituximab over time. Specificity validation included testing for potential cross-reactivity with other antibodies or proteins; however, detailed data on cross-reactivity are limited. The assay was designed to ensure the consistent

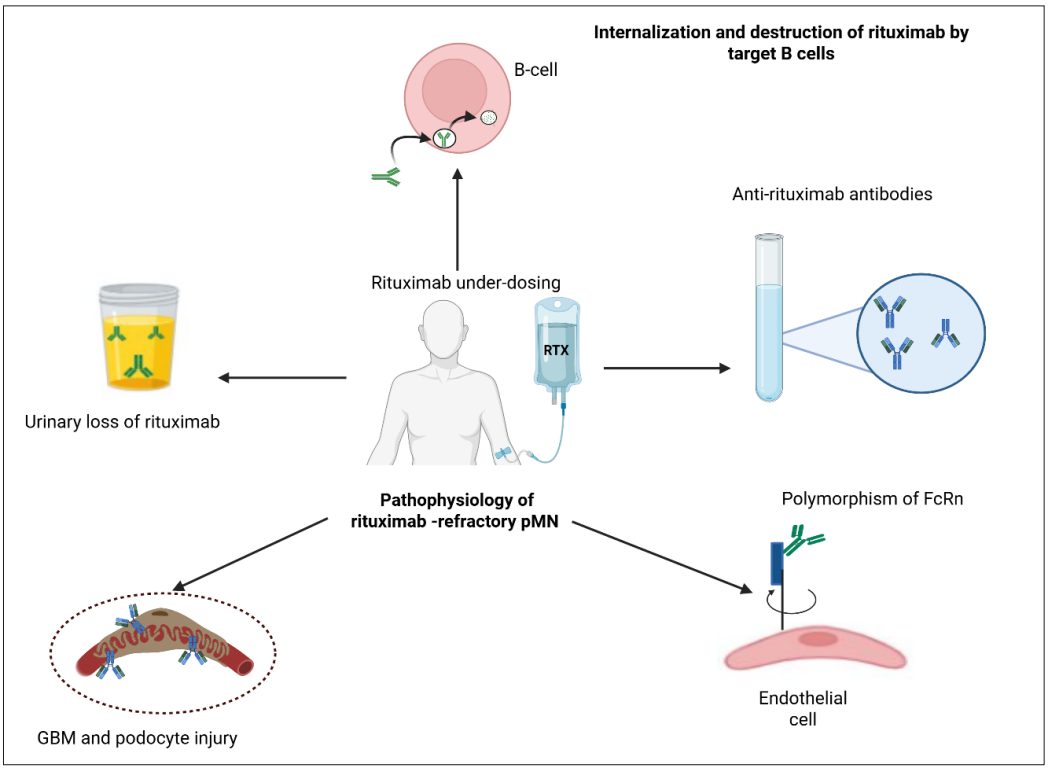

Figure 1. Key factors contributing to rituximab under-dosing in primary membranous nephropathy. Created in BioRender. https://BioRender.com/0nbzd7p.

application of the primary coating antibody in the ELISA, thereby enhancing specificity. The accuracy ranged from 91% to 125% for within-day measurements and 95% to 109% for between-day measurements. This level of accuracy confirms the reliability of ELISA in quantifying rituximab concentrations. Current evidence supports ELISA-based rituximab quantification as a method with promising sensitivity and specificity, making it valuable for pharmacokinetic studies and therapeutic monitoring in clinical trials. Furthermore, the precision of this assay in measuring rituximab levels can aid in optimizing dosage regimens (45,46).

Flow cytometry

The determination of B lymphocyte levels and their functional subsets has greatly advanced over the past decade owing to improvements in flow cytometry techniques (38). Modern high-sensitivity, multi-color flow cytometry methods now allow the detection and enumeration of very small quantities of B cells and B cell subsets in the peripheral blood of patients receiving anti-CD20 mAb therapy (15). Roland Jacobs et al applied a flow cytometric technique to measure the concentration of monoclonal antibodies in urine samples. They analyzed 12 urine samples from patients with confirmed nephrotic syndrome who had undergone rituximab treatment. A 0.8 g/L rituximab solution was serially diluted to create the standards. Using the samples' mean fluorescence intensity to construct a standard curve, the results showed an R-squared value of 0.998, a y-intercept of 379.3, and a slope of 12.71. The high sensitivity of the assay was confirmed by the clear detection of as little as 12.5 μg/L of rituximab. The strong correlation between the mean fluorescence intensity of tagged cells and the actual rituximab concentration, demonstrated by an R-squared value of 0.998, highlights the reliability of this assay (47). The monitoring of rituximab levels under different clinical situations is summarized in Table 2.

Conclusion

Given the significant drug loss in urine, antibody detection, incorporation, and destruction of rituximab by target B cells, as well as polymorphisms of the FcRn for IgG, which may impede B-cell depletion and delay remission, rituximab levels must be closely monitored in patients undergoing treatment for pMN. Regular monitoring facilitates consistent treatment regimens, thereby reducing the risk of both under-treatment and overtreatment. In addition to monitoring anti-PLA2R antibodies, regular assessment of rituximab levels may

Table 2. Rituximab level monitoring across various clinical conditions

Author/year	Disease	Drug and dose	Method used	Results
Berinstein et al, 1988 (48)	Follicular or low-grade NHL	RTX 375 mg/m². Four doses were administered once weekly for 22 days.	ELISA	Patients with higher serum rituximab levels exhibited better treatment responses. Responders consistently had greater median serum rituximab levels than non-responders at all evaluated time points. Elevated serum rituximab levels may promote more effective tumor regression and indicate a smaller tumor burden, which is a favorable prognostic factor. This suggests that rituximab efficacy depends on both the actual serum antibody concentration and tumor size.
Liu et al, 2022 (49)	NHL	510 Samples from a B-cell non-Hodgkin's lymphoma. RTX 375 mg/m² triweekly.	ELISA	Low C1-trough levels are associated with unfavorable clinical outcomes, including shorter overall survival and disease progression. Conversely, higher C1-trough levels reduce high-risk factors and are associated with better treatment responses.
Mazilu et al, 2014 (50)	RA	62 patients receiving RTX for RA	ELISA	Patients with detectable RTX levels exhibited better clinical responses at subsequent evaluations, with significant differences in disease activity scores (DAS28 and SDAI) between those with and without detectable RTX levels.
Cohen and Keystone, 2015 (51)	ANCA-vasculitis	89 patients treated with RTX, four weekly infusions of 375 mg/m²	ELISA	Newly diagnosed patients with AAV exhibit lower serum RTX levels. Male patients had significantly lower RTX levels than female patients. Patients who achieved complete remission at six months demonstrate comparable RTX serum levels. No significant association was found between RTX levels and time to relapse. Prolonged B cell depletion is often associated with higher RTX serum concentrations.

Abbreviations: ANCA, Anti-neutrophil cytoplasm antibodies; ELISA, Enzyme-linked immunosorbent assay; RA, Rheumatoid arthritis; RTX, rituximab; SDAI, simplified disease activity Index; DAS28, Disease Activity Score including a 28-joint count; AAV, ANCA-associated vasculitis; NHL, Non-Hodgkin lymphoma.

improve the clinical outcomes of pMN. Further research is required to optimize the dosing strategies.

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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Not applicable. Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

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