KDIGO 2021 Guidelines for Treatment of Glomerular Diseases

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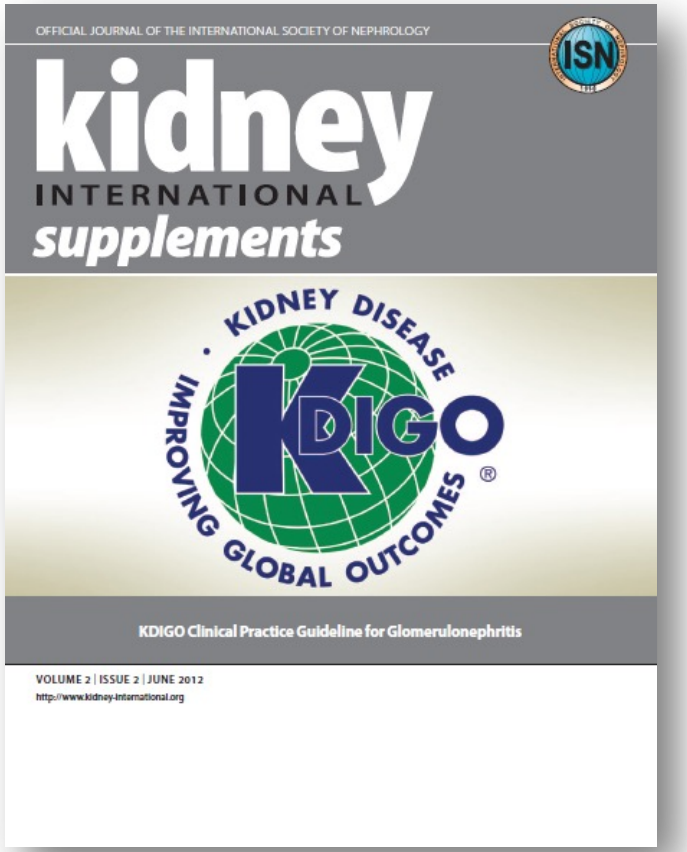
KDIGO GN guidelines



KDIGO executive conclusions www.kidney-international.org

Management and treatment of glomerular diseases (part 1): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

www.kidney-international.org KDIGO executive conclusions

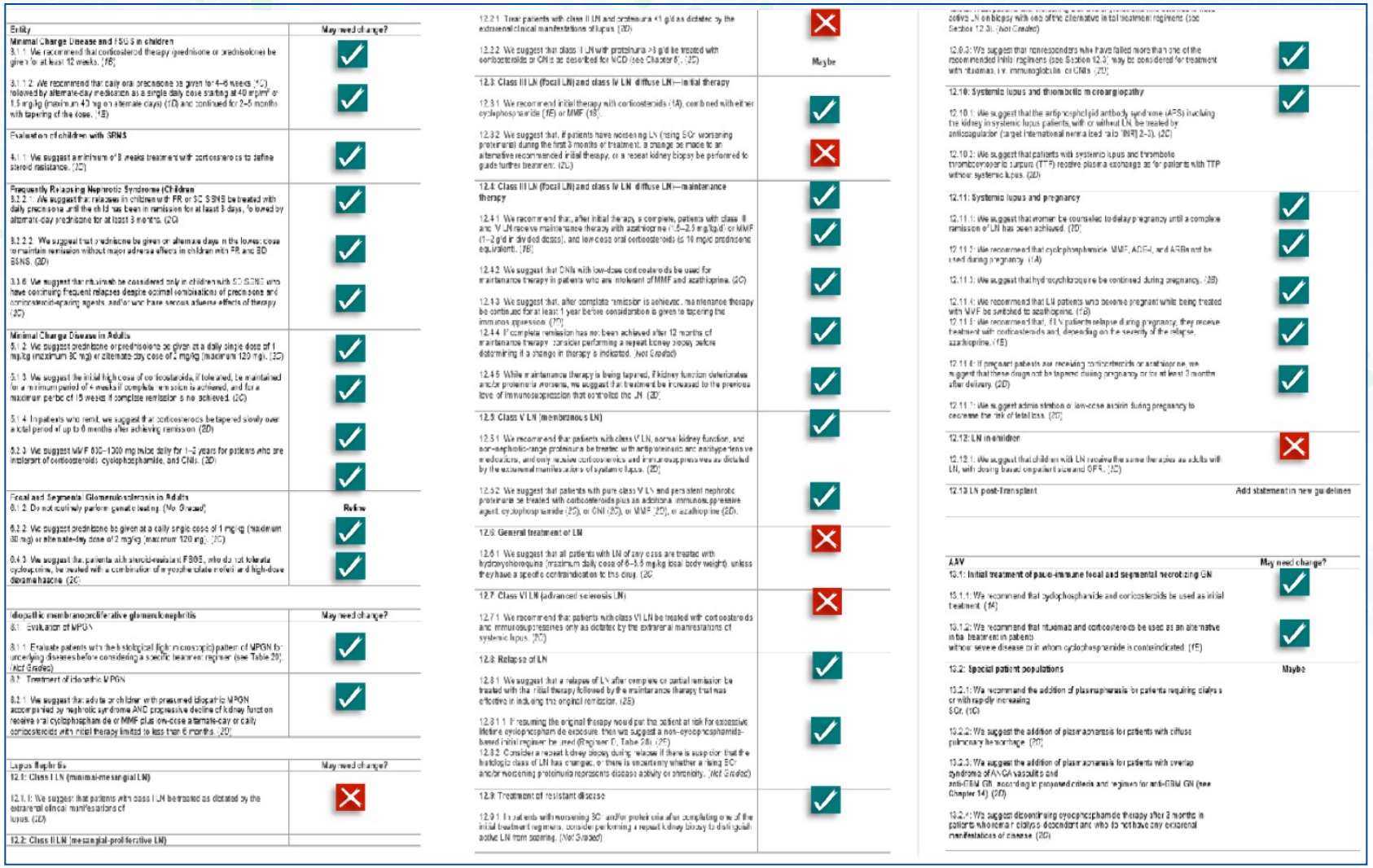
Management and treatment of glomerular diseases (part 2): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

2012 KDIGO guideline document on GNs

2017 Controversies conference on GNs (Singapore)
Published 2018

KEY QUESTION: WHICH OF THE 2012 GLOMERULAR DISEASE GUIDELINE RECOMMENDATIONS NEED REVISION?



Entity	May need change?
Minimal Change Disease and FSGS in children	
3.1.1: We recommend that corticosteroid therapy (prednisone or prednisolone) be given for at least 12 weeks. (1B)	✓
3.1.1.2: We recommend that daily oral prednisone be given for 4–6 weeks (1C), followed by alternate-day medication as a single daily dose starting at 40 mg/m² or 1.5 mg/kg (maximum 40 mg on alternate days) (1D) and continued for 2–5 months with tapering of the dose. (1B)	✓
Evaluation of children with SRNS	
3.1.1: We suggest a minimum of 8 weeks treatment with corticosteroids to define steroid resistance. (2D)	✓
Frequently Relapsing Nephrotic Syndrome (Children	
3.2.2.1: We suggest that relapses in children with FR or SC SRNS be treated with daily prednisone until the child has been in remission for at least 3 days, followed by alternate-day prednisone for at least 3 months. (2C)	✓
3.2.2.2: We suggest that cyclosporine be given or alternative drugs in the lowest dose to maintain remission without major adverse effects in children with FR and SD SRNS. (2D)	✓
3.3.6: We suggest that rituximab be considered only in children with SD SRNS who have continuing frequent relapses despite optimal combinations of prednisone and corticosteroid-sparing agents, and/or who have serious adverse effects of therapy (2C)	✓
Minimal Change Disease in Adults	
5.1.2: We suggest prednisone or prednisolone be given at a daily single dose of 1 mg/kg (maximum 80 mg) or alternate-day dose of 2 mg/kg (maximum 120 mg). (2D)	✓
5.1.3: We suggest the initial high dose of corticosteroids, if tolerated, be maintained for a minimum period of 4 weeks if complete remission is achieved, and for a maximum period of 16 weeks if complete remission is not achieved. (2C)	✓
5.1.4: In patients who remit, we suggest that corticosteroids be tapered slowly over a total period of up to 6 months after achieving remission (2D)	✓
5.2.3: We suggest MMF 500–1000 mg twice daily for 1–2 years for patients who are intolerant of corticosteroids, cyclophosphamide, and CNIs. (2D)	✓
Focal and Segmental Glomerulosclerosis in Adults	**Refine**
6.1.2: Do not routinely perform genetic testing. (Not Graded)	
6.2.2: We suggest prednisone be given at a daily single dose of 1 mg/kg (maximum 80 mg) or alternate-day dose of 2 mg/kg (maximum 120 mg). (2C)	✓
6.4.3: We suggest that patients with steroid-resistant FSGS, who do not tolerate cyclosporine, be treated with a combination of enzyme-inhibitor and high-dose dexamethasone. (2C)	✓

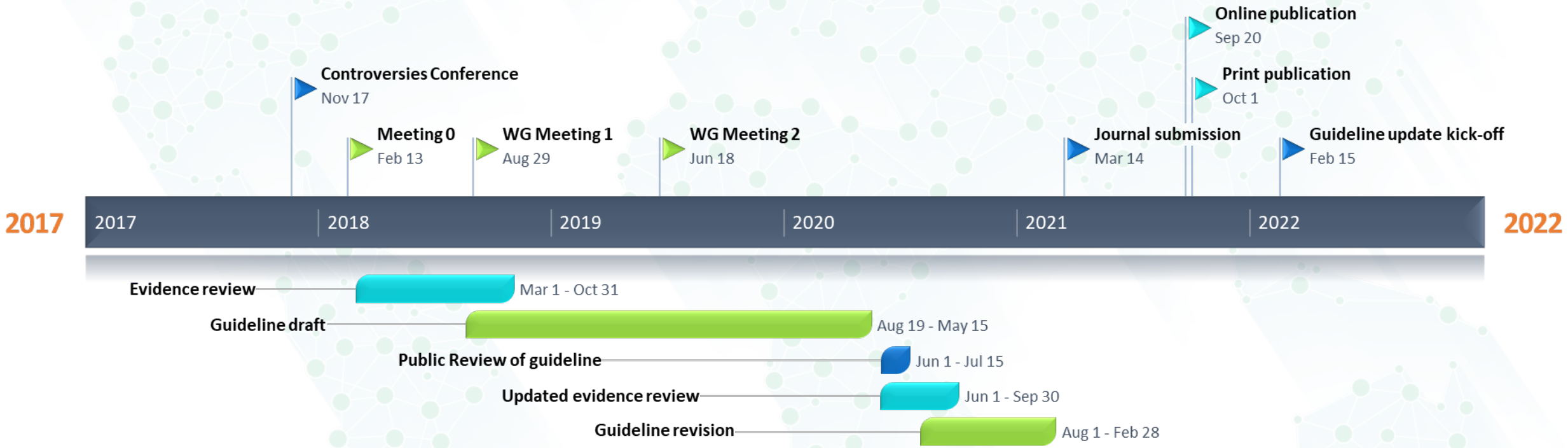
Idiopathic membranoproliferative glomerulonephritis	May need change?
8.1: Evaluation of MPGN	
8.1.1: Evaluate patients with the histological light microscopic pattern of MPGN for underlying diseases before considering a specific treatment regimen (see Table 29). (Not Graded)	✓
8.2: Treatment of Idiopathic MPGN	
8.2.1: We suggest that adults or children with presumed idiopathic MPGN accompanied by nephrotic syndrome AND progressive decline of kidney function receive oral cyclophosphamide or MMF plus low-dose alternate-day or daily corticosteroids with initial therapy limited to less than 6 months. (2D)	✓

Lupus Nephritis	May need change?
12.1: Class I LN (minimal-mesangial LN)	
12.1.1: We suggest that patients with class I LN be treated as dictated by the extrarenal clinical manifestations of lupus. (2D)	✗
12.2: Class II LN (mesangial-proliferative LN)	
12.2.1: Treat patients with class II LN and proteinuria <1 g/d as dictated by the extrarenal clinical manifestations of lupus. (2D)	✗
12.2.2: We suggest that class II LN with proteinuria >1 g/d be treated with corticosteroids or CNIs as described for MCD (see Chapter 6). (2D)	Maybe
12.3: Class III LN (focal LN) and class IV LN diffuse LN—initial therapy	
12.3.1: We recommend initial therapy with corticosteroids (1A), combined with either cyclophosphamide (1B) or MMF (1B).	✓
12.3.2: We suggest that, if patients have worsening LN (rising SCr, worsening proteinuria) during the first 3 months of treatment, a change be made to an alternative recommended initial therapy, or a repeat kidney biopsy be performed to guide further treatment. (2C)	✗
12.4: Class III LN (focal LN) and class IV LN diffuse LN—maintenance therapy	✓
12.4.1: We recommend that, after initial therapy is complete, patients with class III and IV LN receive maintenance therapy with azathioprine (1.5–2.5 mg/kg/d) or MMF (1–2 g/d in divided doses), and low-dose oral corticosteroids (≤ 10 mg/d prednisone equivalent). (1B)	✓
12.4.2: We suggest that CNIs with low-dose corticosteroids be used for maintenance therapy in patients who are intolerant of MMF and azathioprine. (2C)	✓
12.4.3: We suggest that, after complete remission is achieved, maintenance therapy be continued for at least 1 year before consideration is given to tapering the immunosuppression. (2D)	✓
12.4.4: If complete remission has not been achieved after 12 months of maintenance therapy, consider performing a repeat kidney biopsy before determining if a change in therapy is indicated. (Not Graded)	✓
12.4.5: While maintenance therapy is being tapered, if kidney function deteriorates and/or proteinuria worsens, we suggest that treatment be increased to the previous level of immunosuppression that controlled the LN. (2D)	✓
12.5: Class V LN (membranous LN)	✓
12.5.1: We recommend that patients with class V LN, normal kidney function, and non-nephrotic-range proteinuria be treated with antiproteinuric and antihypertensive medications, and only receive corticosteroids and immunosuppressives as dictated by the extrarenal manifestations of systemic lupus. (2D)	
12.5.2: We suggest that patients with pure class V LN and persistent nephrotic proteinuria be treated with corticosteroids plus an additional immunosuppressive agent: cyclophosphamide (2D), or CNI (2D), or MMF (2D), or azathioprine (2D).	✓
12.6: General treatment of LN	✗
12.6.1: We suggest that all patients with LN of any class are treated with hydroxychloroquine (maximum daily dose of 6.5 mg/kg ideal body weight), unless they have a specific contraindication to this drug. (2C)	
12.7: Class VI LN (advanced sclerosis LN)	✗
12.7.1: We recommend that patients with class VI LN be treated with corticosteroids and immunosuppressives only as dictated by the extrarenal manifestations of systemic lupus. (2C)	
12.8: Relapse of LN	✓
12.8.1: We suggest that a relapse of LN after complete or partial remission be treated with the initial therapy followed by the maintenance therapy that was effective in inducing the original remission. (2B)	
12.8.1.1: If resuming the original therapy would put the patient at risk for excessive lifetime cyclophosphamide exposure, then we suggest a non-cyclophosphamide-based initial regimen be used (Regimen D, Table 28). (2B)	✓
12.8.2: Consider a repeat kidney biopsy during relapse if there is suspicion that the histologic class of LN has changed, or there is uncertainty whether arising SCr and/or worsening proteinuria represents disease activity or chronicity. (Not Graded)	
12.9: Treatment of resistant disease	✓
12.9.1: In patients with worsening SCr and/or proteinuria after completing one of the initial treatment regimens, consider performing a repeat kidney biopsy to distinguish active LN from scarring. (Not Graded)	

12.9.3: We suggest that nonresponders who have failed more than one of the recommended initial regimens (see Section 12.3) may be considered for treatment with rituximab, i.v. immunoglobulin, or CNIs. (2D)	✓
12.10: Systemic lupus and thrombotic microangiopathy	✓
12.10.1: We suggest that the antiphospholipid antibody syndrome (APS) including the kidney in systemic lupus patients, with or without LN, be treated by anticoagulation (target International normalized ratio [INR] 2–3). (2C)	
12.10.2: We suggest that patients with systemic lupus and thrombotic thrombocytopenic purpura (TTP) receive plasma exchange as for patients with TTP without systemic lupus. (2D)	
12.11: Systemic lupus and pregnancy	✓
12.11.1: We suggest that women be counseled to delay pregnancy until a complete remission of LN has been achieved. (2D)	✓
12.11.2: We recommend that cyclophosphamide, MMF, ACEI, and ARBs not be used during pregnancy. (1A)	
12.11.3: We suggest that hydroxychloroquine be continued during pregnancy. (2B)	✓
12.11.4: We recommend that LN patients who become pregnant while being treated with MMF be switched to azathioprine. (1B)	✓
12.11.5: We recommend that, if LN patients relapse during pregnancy, they receive treatment with corticosteroids and, depending on the severity of the relapse, azathioprine. (1B)	✓
12.11.6: If pregnant patients are receiving corticosteroids or azathioprine, we suggest that these drugs not be tapered during pregnancy or for at least 3 months after delivery. (2D)	✓
12.11.7: We suggest administration of low-dose aspirin during pregnancy to decrease the risk of fetal loss. (2C)	
12.12: LN in children	✗
12.12.1: We suggest that children with LN receive the same therapies as adults with LN, with dosing based on patient size and GFR. (2C)	
12.13 LN post-transplant	Add statement in new guidelines

ANV	May need change?
13.1: Initial treatment of pauci-immune focal and segmental necrotizing GN	✓
13.1.1: We recommend that cyclophosphamide and corticosteroids be used as initial treatment. (1A)	
13.1.2: We recommend that rituximab and corticosteroids be used as an alternative initial treatment in patients without severe disease or in whom cyclophosphamide is contraindicated. (1B)	✓
13.2: Special patient populations	Maybe
13.2.1: We recommend the addition of plasmapheresis for patients requiring dialysis or with rapidly increasing SCr. (1C)	
13.2.2: We suggest the addition of plasmapheresis for patients with diffuse pulmonary hemorrhage. (2C)	
13.2.3: We suggest the addition of plasmapheresis for patients with overlap syndromes of ANCA vasculitis and anti-GBM GN, according to proposed criteria and regimens for anti-GBM GN (see Chapter 14). (2D)	
13.2.4: We suggest discontinuing cyclophosphamide therapy after 3 months in patients who remain dialysis dependent and who do not have any extrarenal manifestations of disease. (2D)	

Timeline of Guideline for Management of GD



WORK GROUP

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

SUPPLEMENT TO

kidney INTERNATIONAL

KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases

VOLUME 100 | ISSUE 4S | OCTOBER 2021
www.kidney-international.org

What Is New Since the 2012 KDIGO Guideline

- General principles chapter discusses supportive therapies appropriate for all GD that supplement the more specific immunosuppressive treatments for each disease.
- Membranous nephropathy chapter now provides an in-depth discussion of monitoring pathogenic autoantibodies in disease management.
- MPGN chapter was replaced with a new chapter entitled *Immunoglobulin- and complement-mediated glomerular diseases with an MPGN pattern of injury*.
- ANCA-associated vasculitis chapter compares and contrasts B cell–targeted therapies with traditional cytotoxic drugs.
- FSGS chapter has been reorganized to help clinicians more accurately differentiate between FSGS mediated by a soluble factor that may be amenable to immunosuppression, and conditions with FSGS-like histology, for which immunosuppression should not be used.
- Chapter on nephrotic syndrome in children takes advantage of several new trials that have defined duration of immunosuppression, and has been written to closely align with the International Pediatric Nephrology Association (IPNA) guideline.

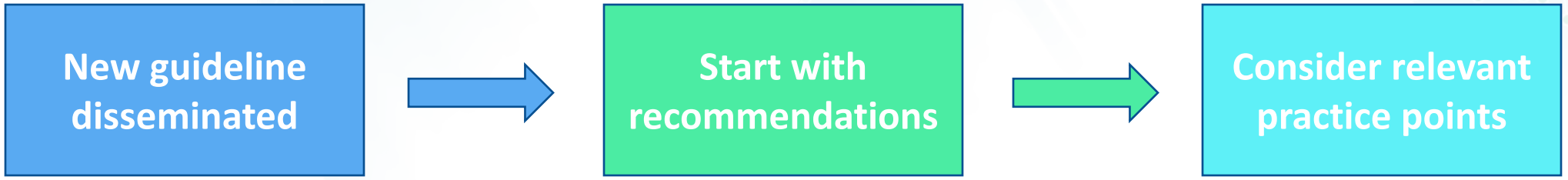
Guideline Format

- KDIGO guidelines continue to use the Grading of Recommendations Assessment, Development, Evaluation (GRADE) methodology, but we have strengthened the link between the recommendation statements and underlying evidence base.
- Guidelines now include a mix of recommendations and “practice points” to help clinicians better evaluate and implement the guidance from the expert Work Group.
- All recommendations follow a consistent and structured format and are similar in style to previous KDIGO recommendations.
- Practice points are a new addition to KDIGO guidance, and may be formatted as a table, a figure, or an algorithm to make them easier to use in clinical practice.

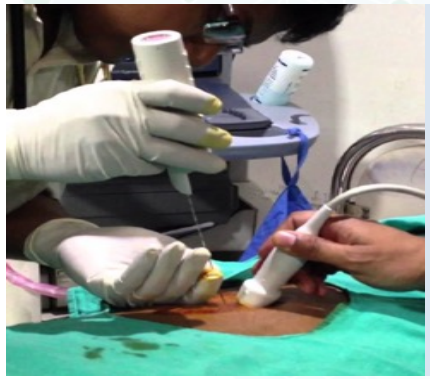
Guideline Format

How should I use practice points when caring for my patients?

- Practice points are consensus statements about a specific aspect of care and supplement recommendations for which a systematic review was conducted.
- Note that practice points represent the expert judgment of the guideline Work Group, but may also be based on limited evidence.
- Unlike recommendations, practice points are not graded for strength of recommendation or quality of the evidence.
- Users should consider the practice point as expert guidance, and use it as they see fit to inform the care of patients.

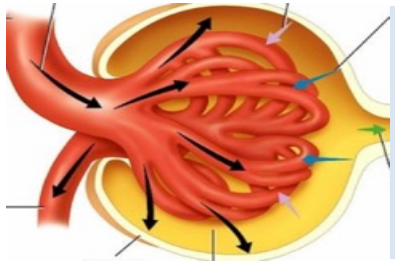


GENERAL MANAGEMENT



- **Kidney biopsy** remains the cornerstone + likely to expand significantly in the near-term
- need for electron microscopy for every biopsy remains controversial

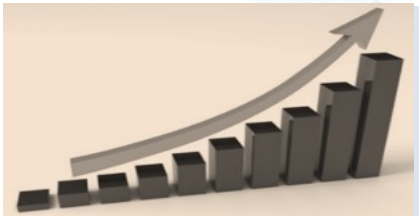
- **ACR and PCR** helpful in general clinical management
- not sufficiently accurate for therapeut. decisions when using high-risk medications



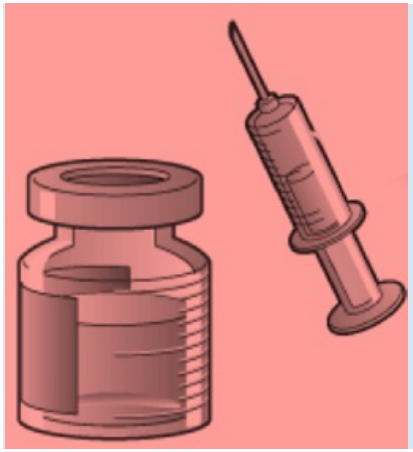
- **eGFR equations** not validated in specific glomerular diseases and patient populations

General Management

- **patient engagement** in determining clinical trial eligibility
- patient-related outcomes and measurements rapidly evolving

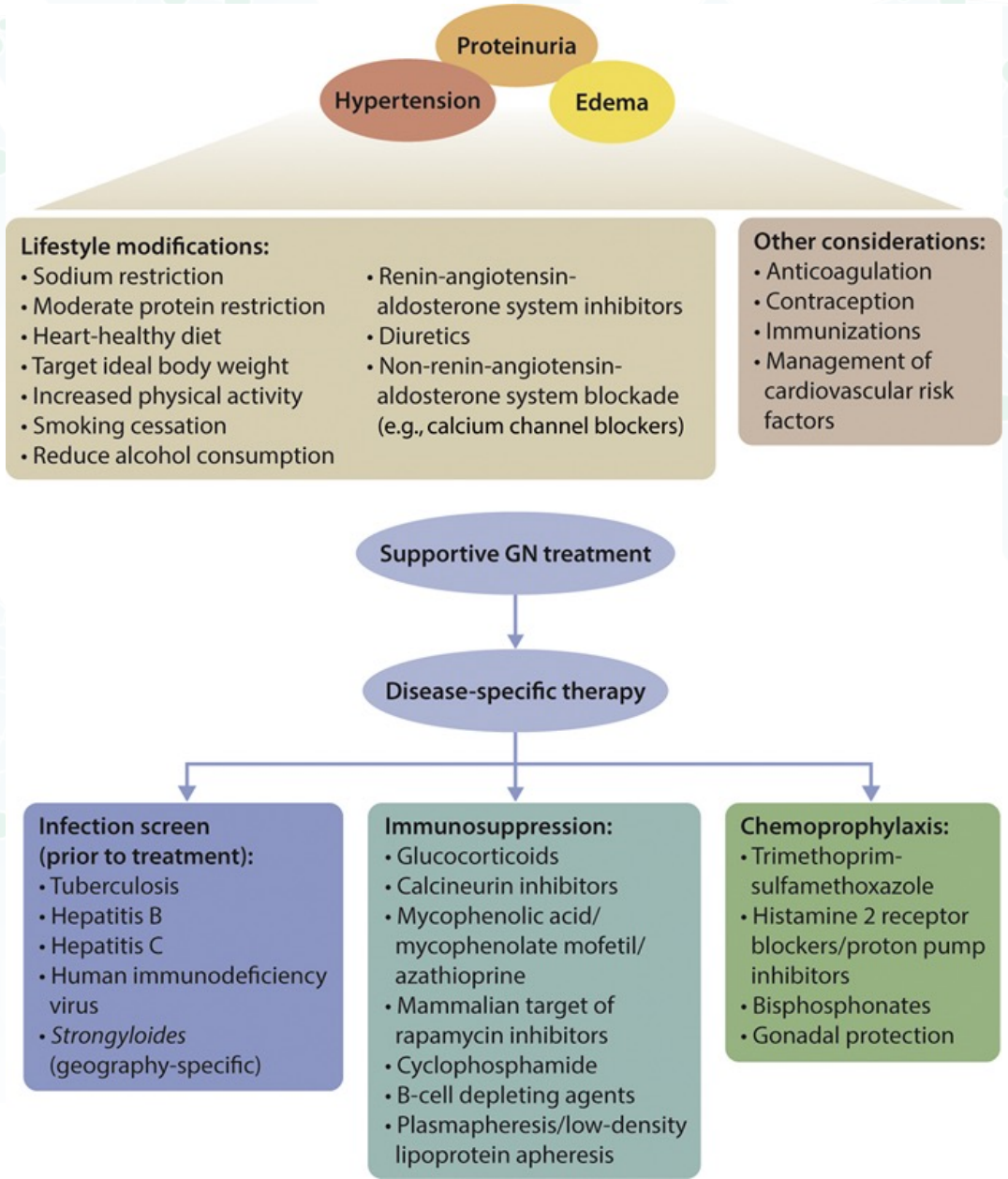


- **Newer determinants of progression**: prematurity, sleep disturbances, obesity, genetics



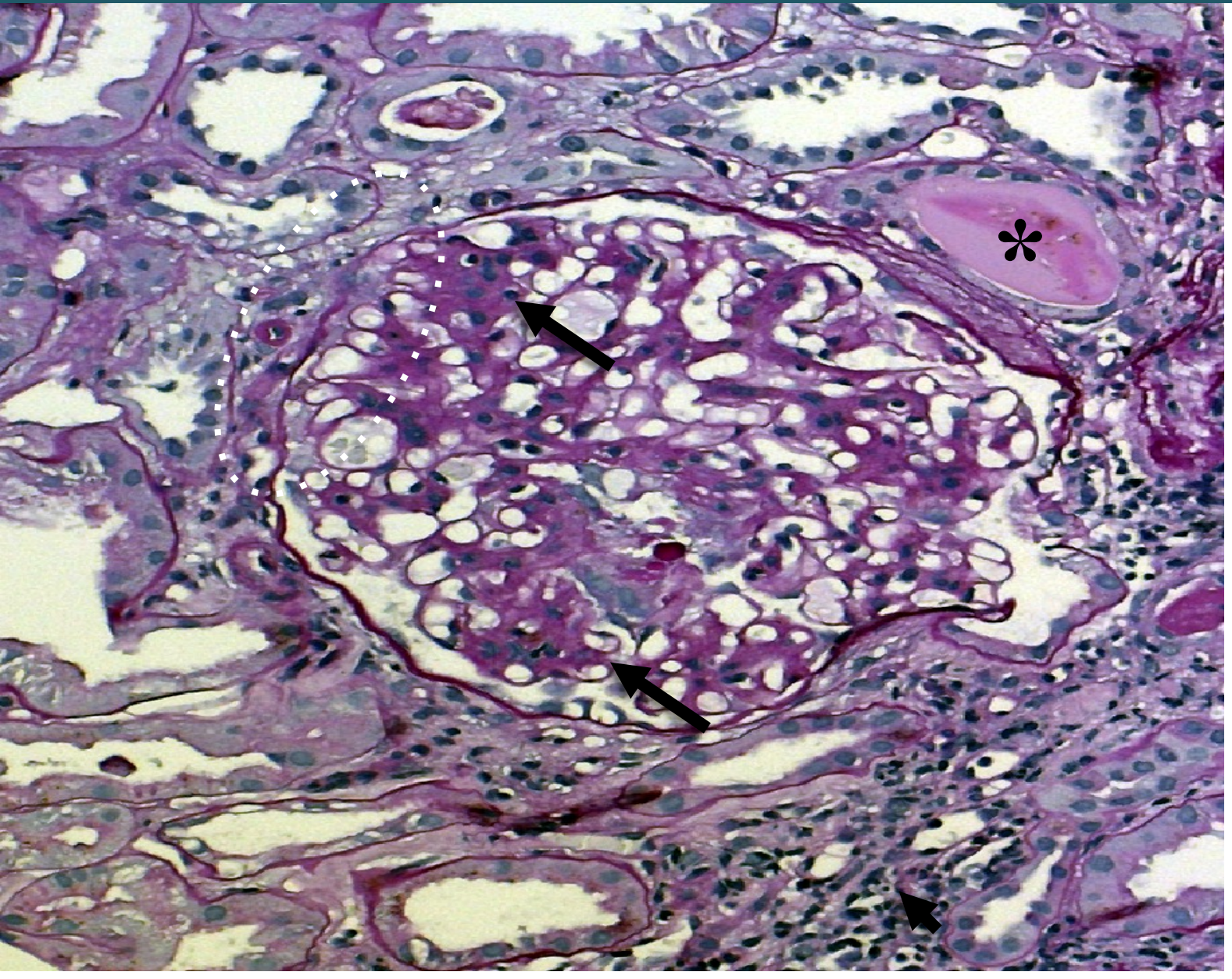
- **Hypertension + proteinuria**: important
- **Uncertain**: aldosterone or SGLT2 blockers; PCSK9 inhibitors and NOAC in nephrotic pts.
- **multidisciplinary support, infection control**
- **Role of prophylactic anticoagulation discussed**

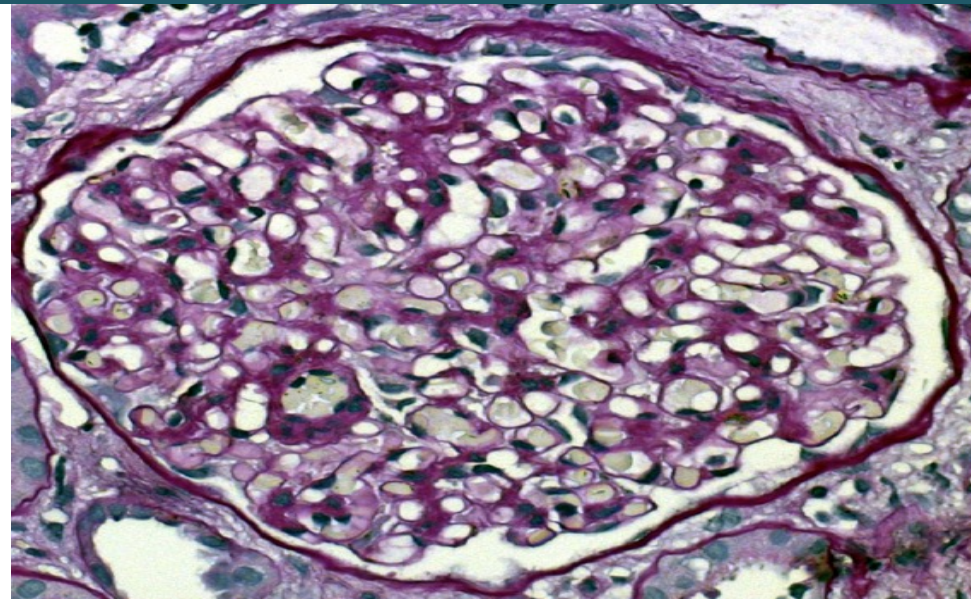
Overview of General Management

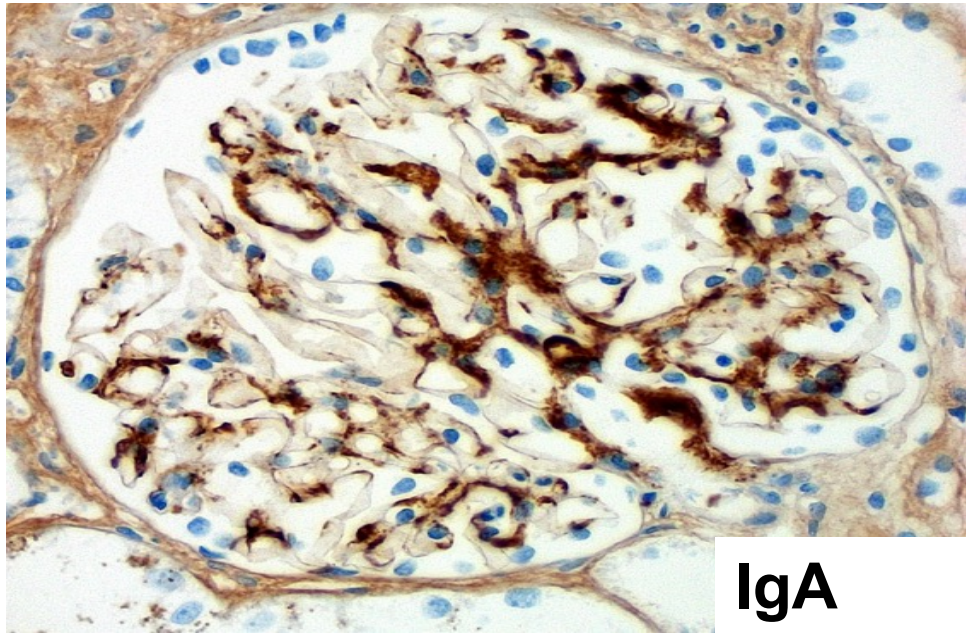


Some specific glomerulonephritides

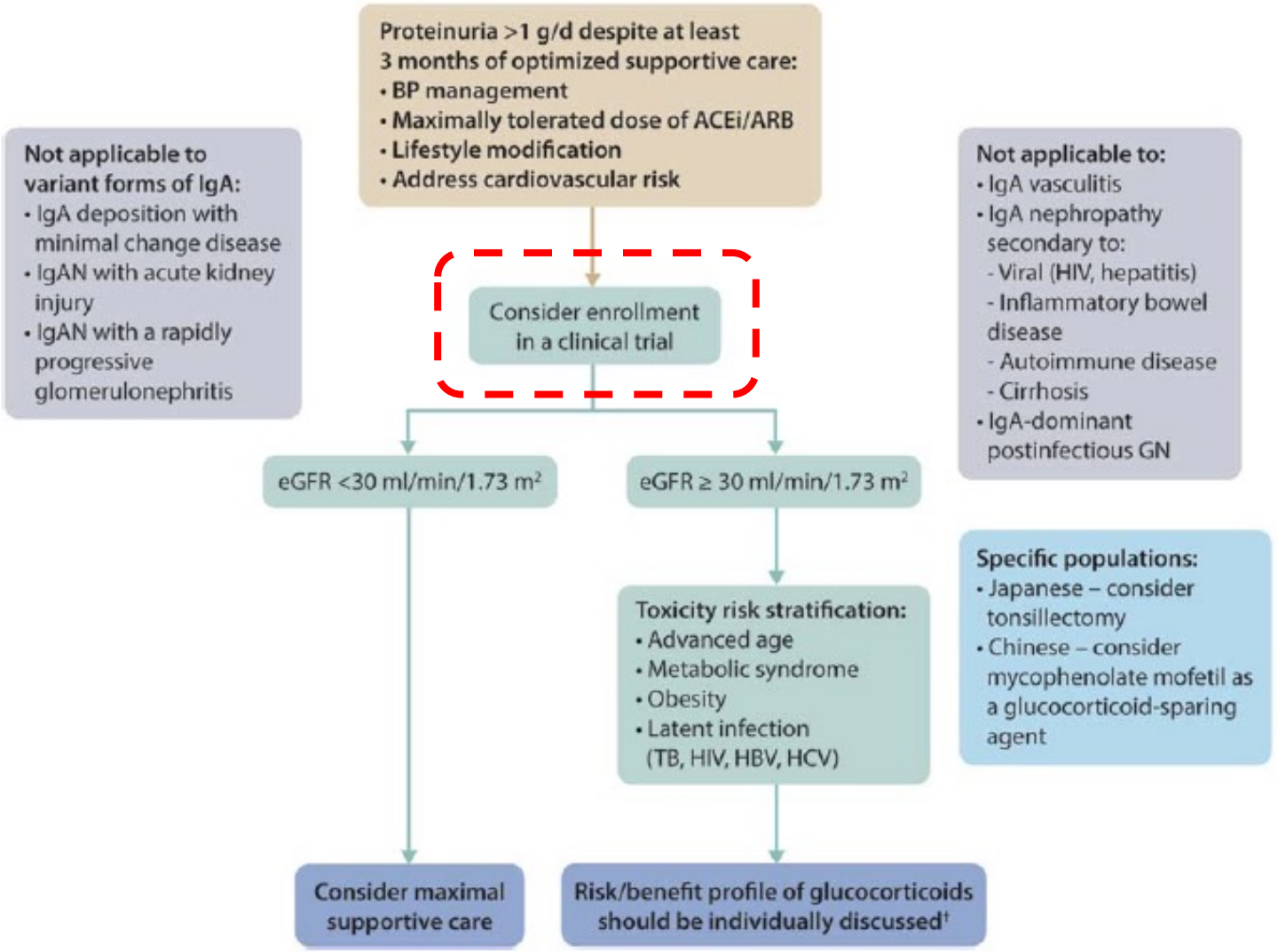
IgA-Nephropathy







Management of patients at risk of progressive disease



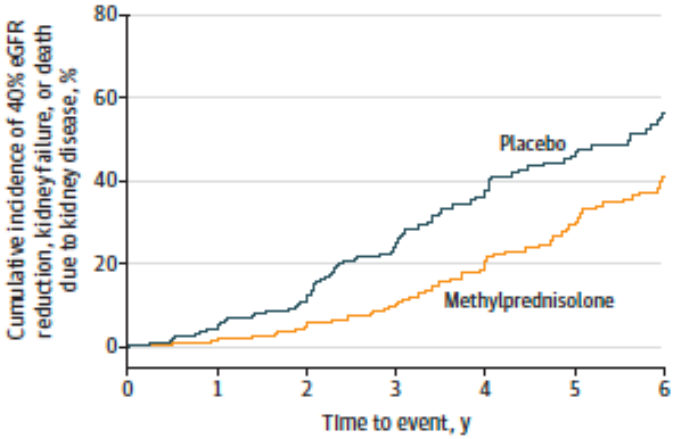
Research

JAMA | Original Investigation

Effect of Oral Methylprednisolone on Clinical Outcomes in Patients With IgA Nephropathy
The TESTING Randomized Clinical Trial

Jicheng Lv, MD; Hong Zhang, PhD; Muh Geot Wong, PhD; Meg J. Jardine, PhD; Michelle Hladunewich, MD; Vivek Jha, MD; Helen Monaghan, PhD; Minghui Zhao, MD; Sean Barbour, MD; Heather Reich, MD; Daniel Cattran, MD; Richard Glassock, MD; Adeera Levin, FRCPC; David Wheeler, FRCP; Mark Woodward, PhD; Laurent Billot, MSc; Tak Mao Chan, MD; Zhi-Hong Liu, MD; David W. Johnson, MD; Alan Cass, FRACP; John Feehally, MD; Jürgen Floege, MD; Giuseppe Remuzzi, MD; Yangfeng Wu, MD; Rajiv Agarwal, MD; Hai-Yan Wang, MD; Vlado Perkovic, PhD; for the TESTING Study Group

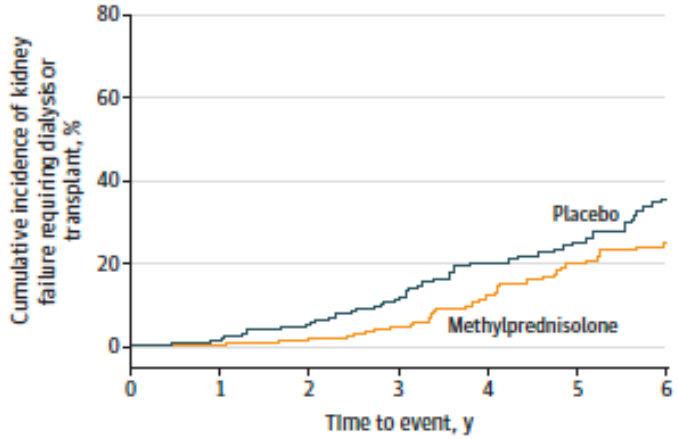
A Primary outcome in all patients



No. of patients at risk

Methylprednisolone	257	250	215	161	105	92	66
Placebo	246	234	188	127	76	66	44

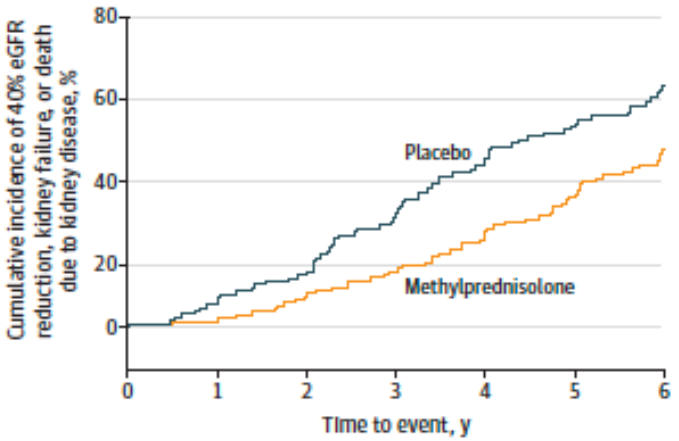
B Kidney failure requiring dialysis or transplant



No. of patients at risk

Methylprednisolone	257	253	223	172	116	103	81
Placebo	246	242	200	147	95	87	62

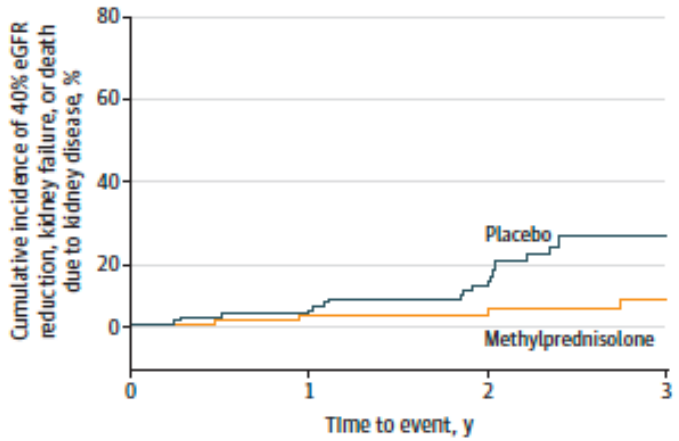
C Primary outcome in full-dose cohort



No. of patients at risk

Methylprednisolone	136	133	124	117	104	92	66
Placebo	126	119	110	92	76	66	44

D Primary outcome in reduced-dose cohort



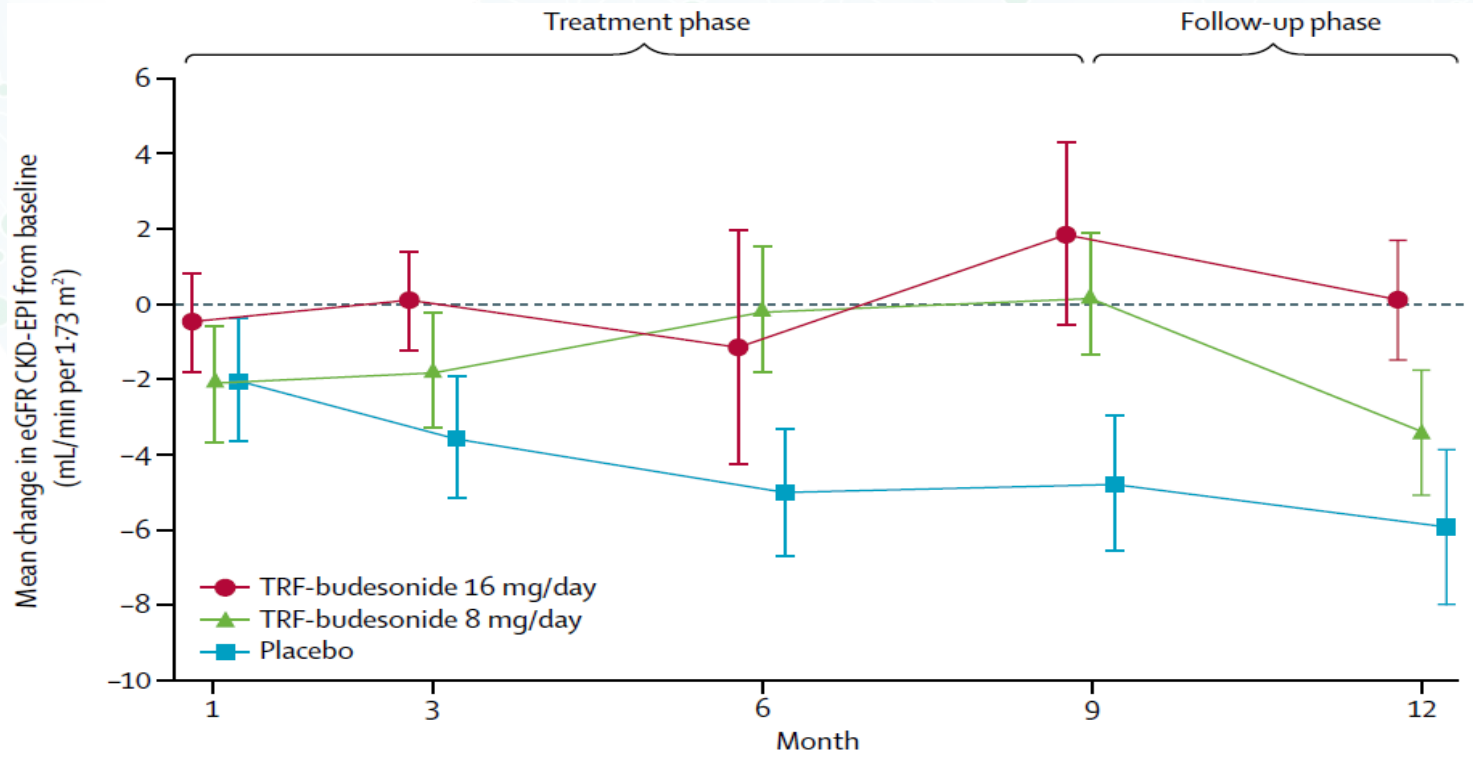
No. of patients at risk

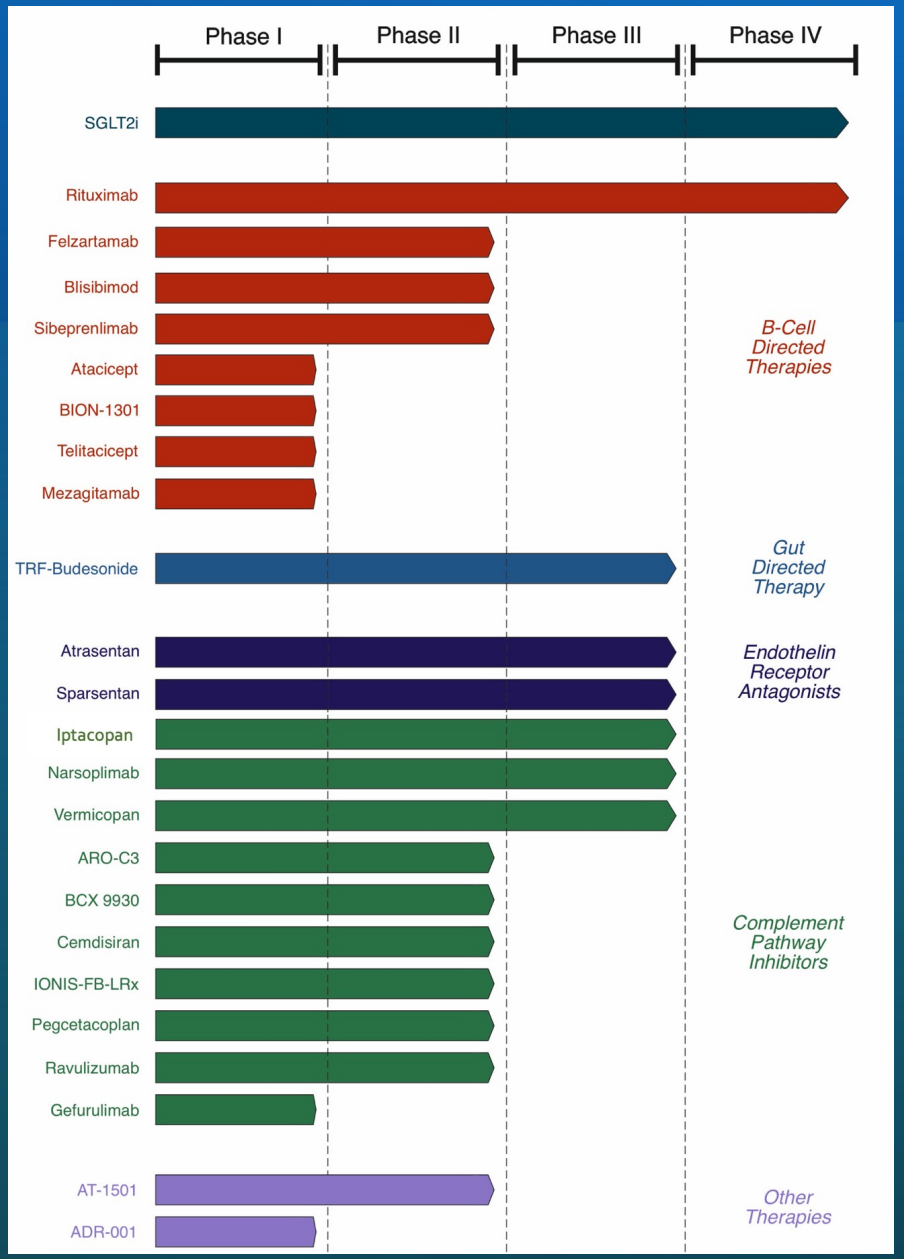
Methylprednisolone	121	117	91	44
Placebo	120	115	78	35

Lancet 2017; 389: 2117–27

Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial

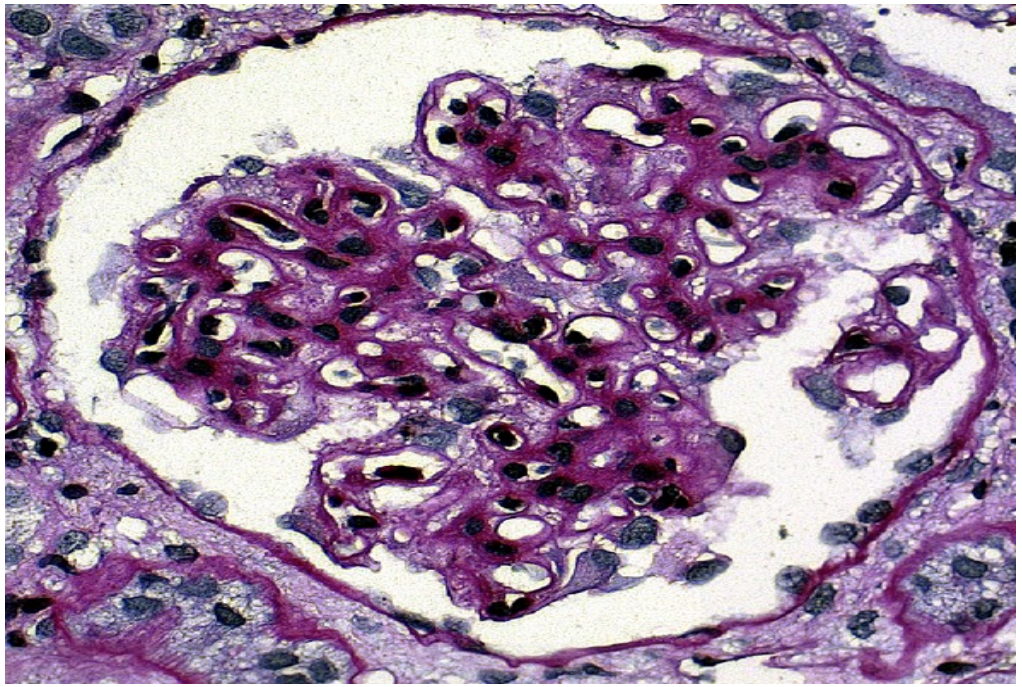
Bengt C Fellström, Jonathan Barratt, Heather Cook, Rosanna Coppo, John Feehally, Johan W de Fijter, Jürgen Floege, Gerd Hetzel, Alan G Jardine, Francesco Locatelli, Bart D Maes, Alex Mercer, Fernanda Ortiz, Manuel Praga, Søren S Sørensen, Vladimir Tesar, Lucia Del Vecchio, for the NEFIGAN Trial Investigators

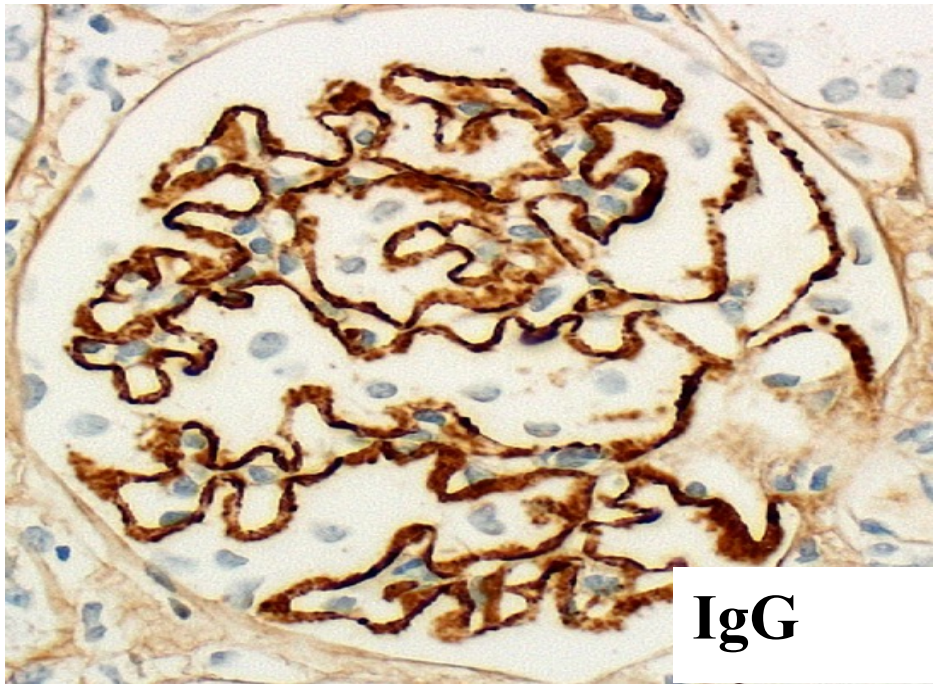


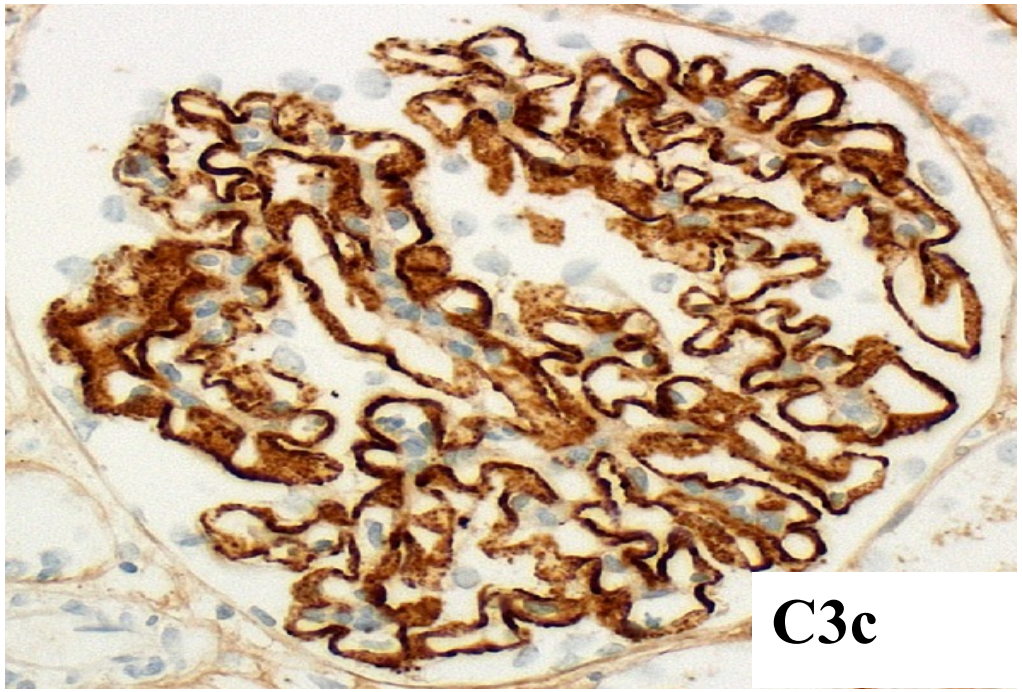


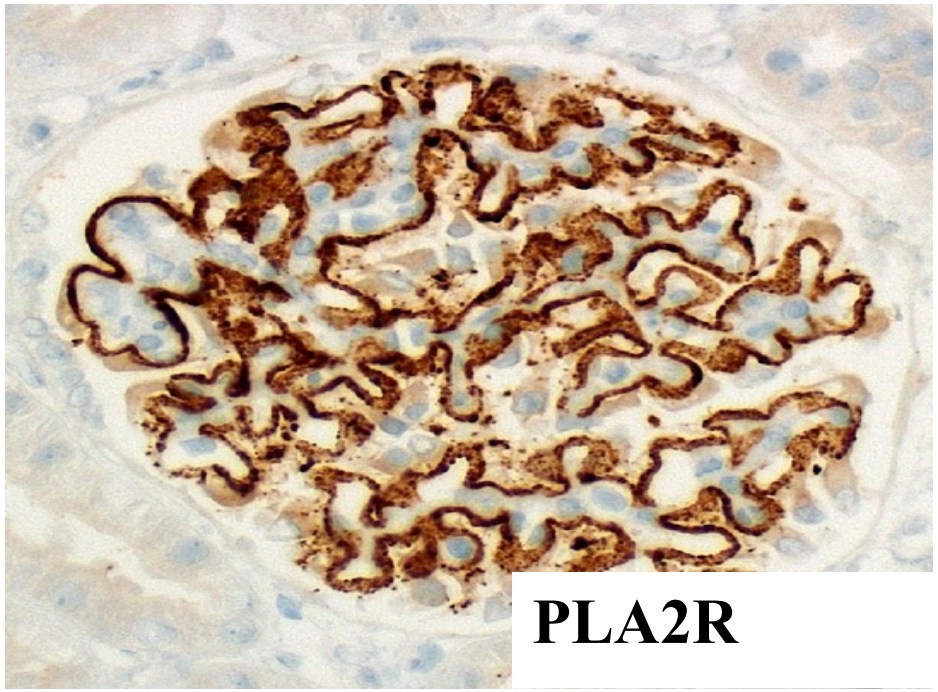
Courtesy Jon Barratt

MEMBRANOUS GN



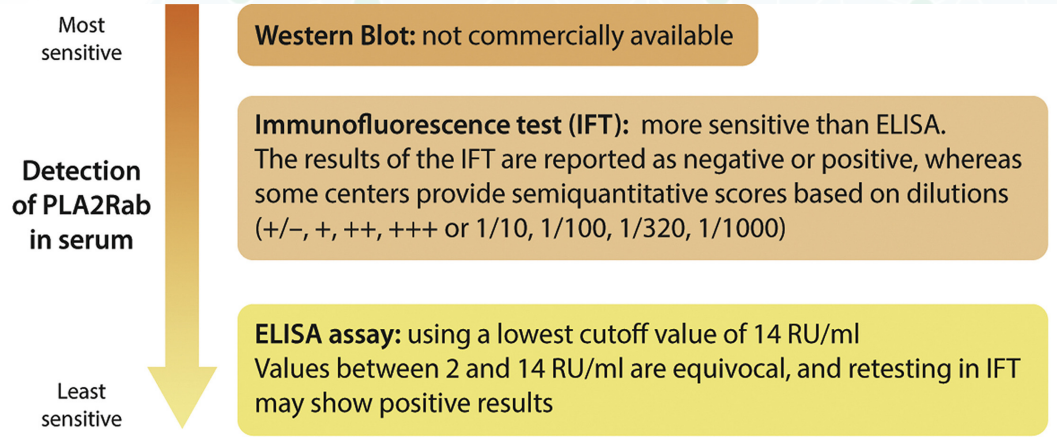


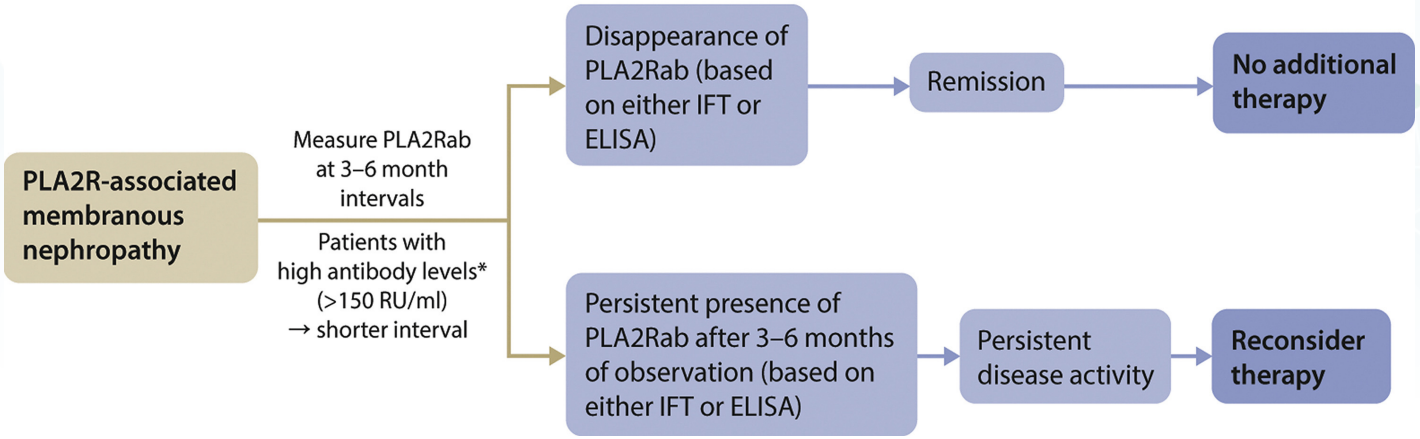




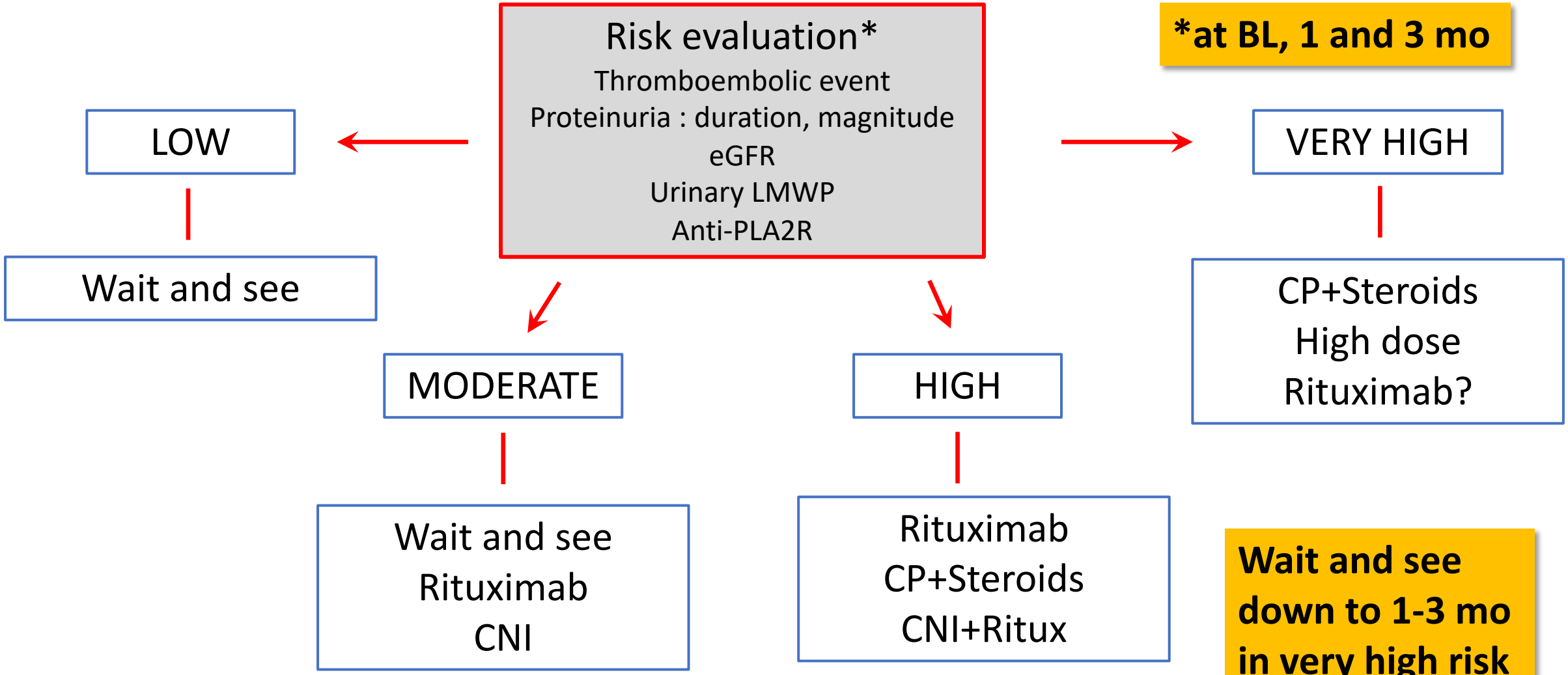
Membranous Nephropathy - Diagnosis

Practice Point 3.1.1: A kidney biopsy is not required to confirm the diagnosis of membranous nephropathy (MN) in patients with nephrotic syndrome and a positive antiPLA2R antibody test.



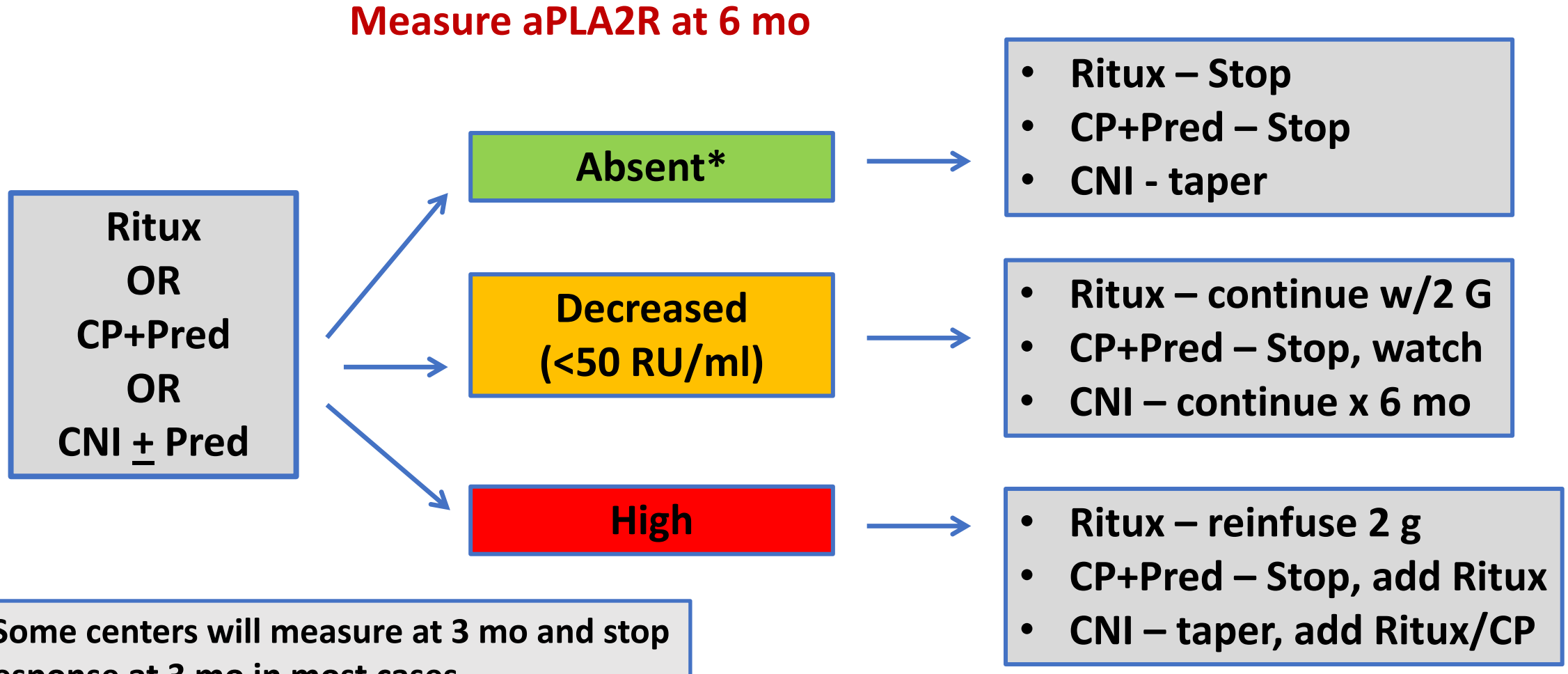


Risk-based initial treatment of MN



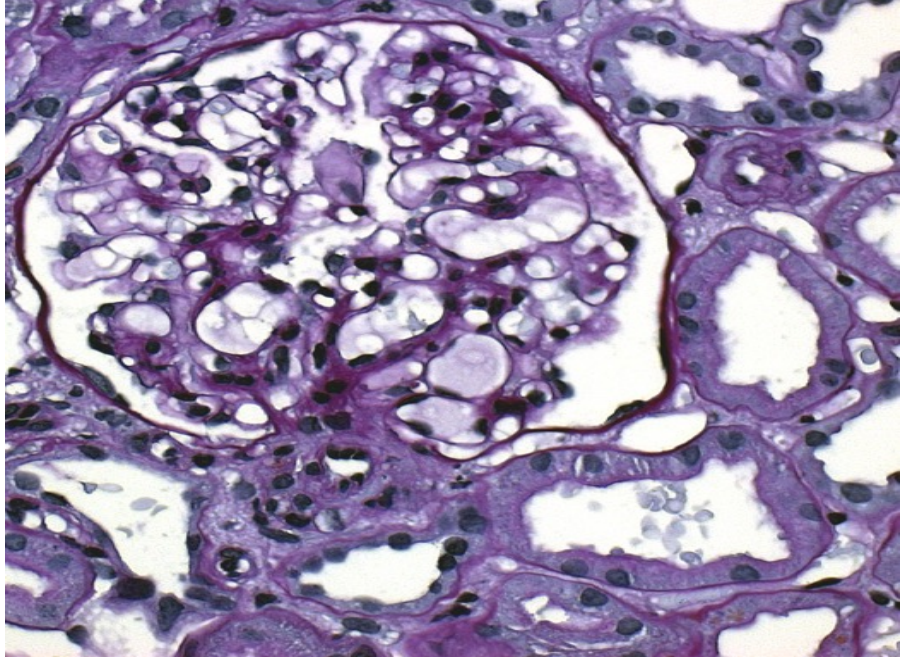
Wetzels J, Ronco P, Jha V. KIS Sep 2021

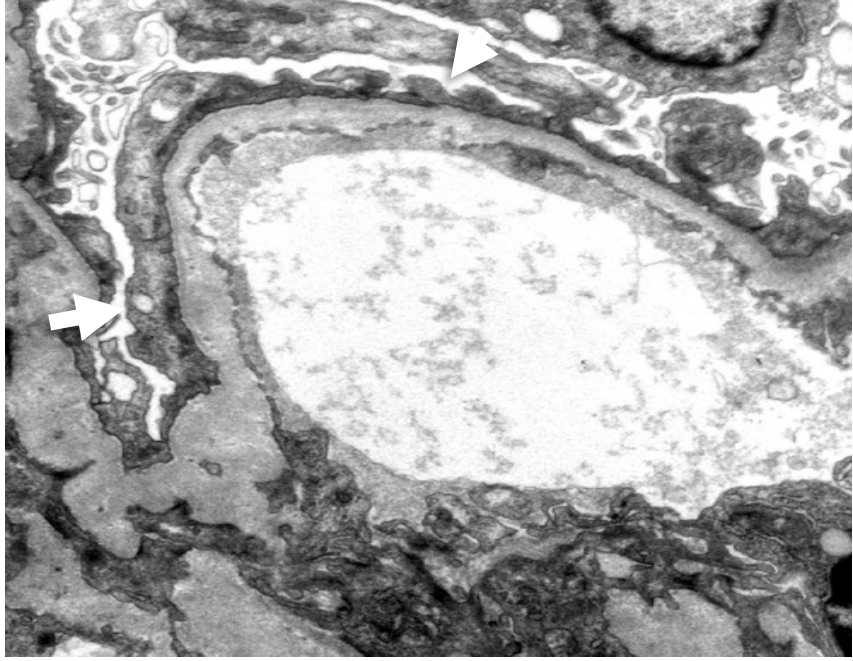
Simplified 2021 KDIGO algorithm for monitoring: Adjust treatment according to aPLA2R trajectory



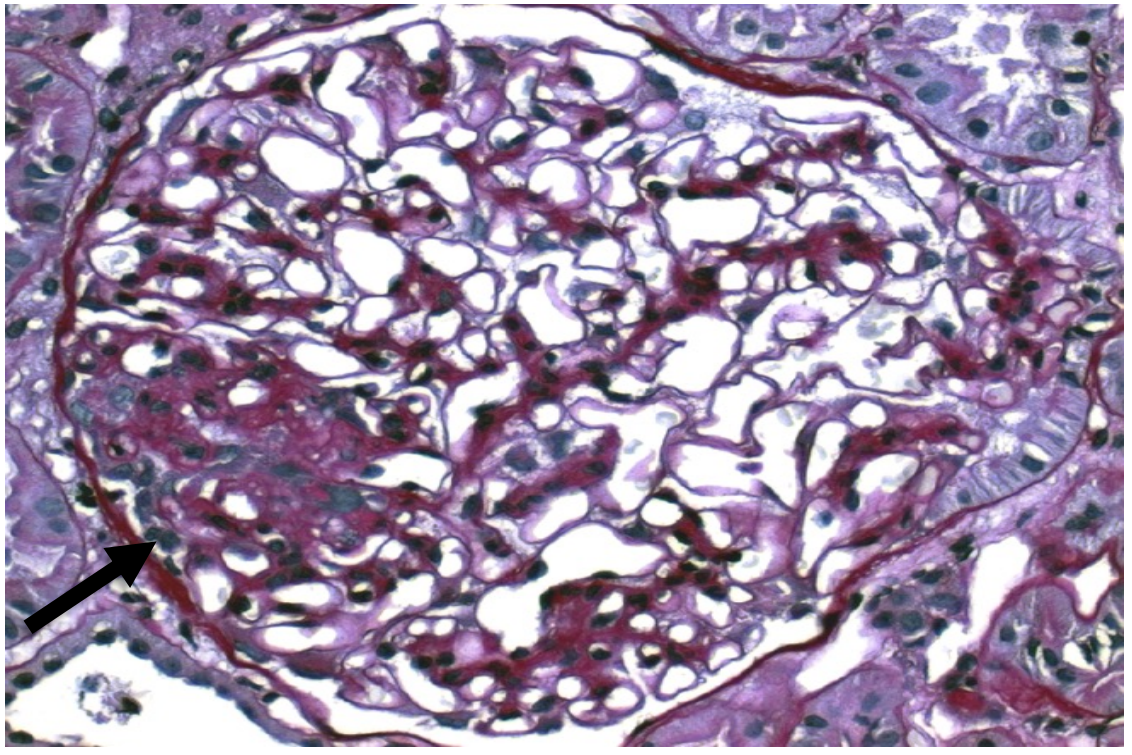
Wetzels J, Ronco P, Jha V. KIS Sep 2021

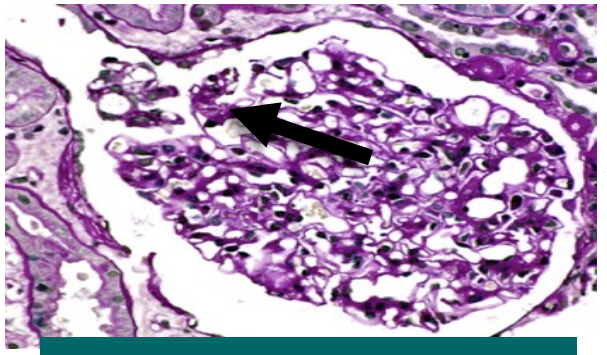
Minimal Change Nephropathy



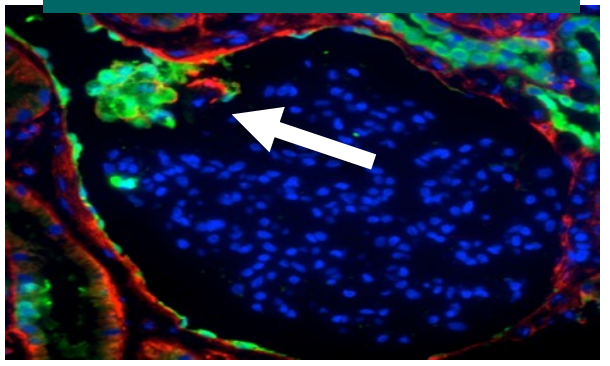


Focal Segmental Glomerulo-sclerosis





Parietal cell activation



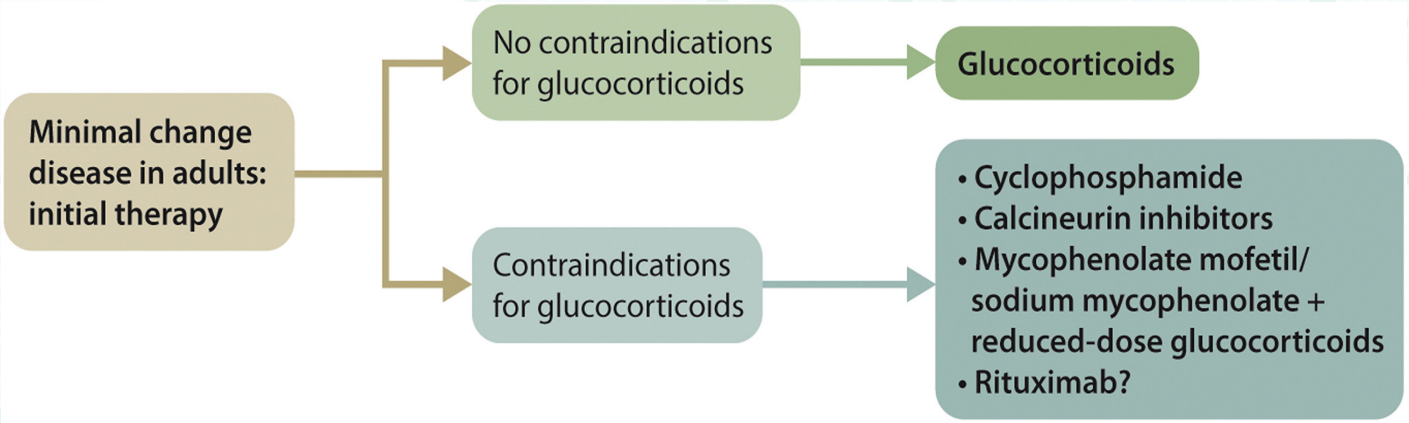
MINIMAL CHANGE GN & FSGS

- **"Steroid sensitive" and "steroid-resistant NS"** should remain
- Term **"primary/idiopathic FSGS"** may require revision.
- **Genetic testing:** patients with congenital/infantile forms of nephrotic syndrome, syndromic features, familial forms
- ***Children***: Steroids first in all nephrotic pts; need for a global definition of "steroid resistance," precise order of CYC, MMF, CNI and rituximab not well determined.
- ***Adults:*** minimum 16 weeks of high-dose steroids as first-line therapy for FSGS or MCD controversial. Several studies indicate that > 8-12 weeks steroids does not reduce relapse. CNIs or CYC second-line agents in adults with MCD. RTX emerging second-line therapy in MCD. CNIs and MMF second- and third-line treatments, resp., for FSGS.

MCD in Adults - Treatment

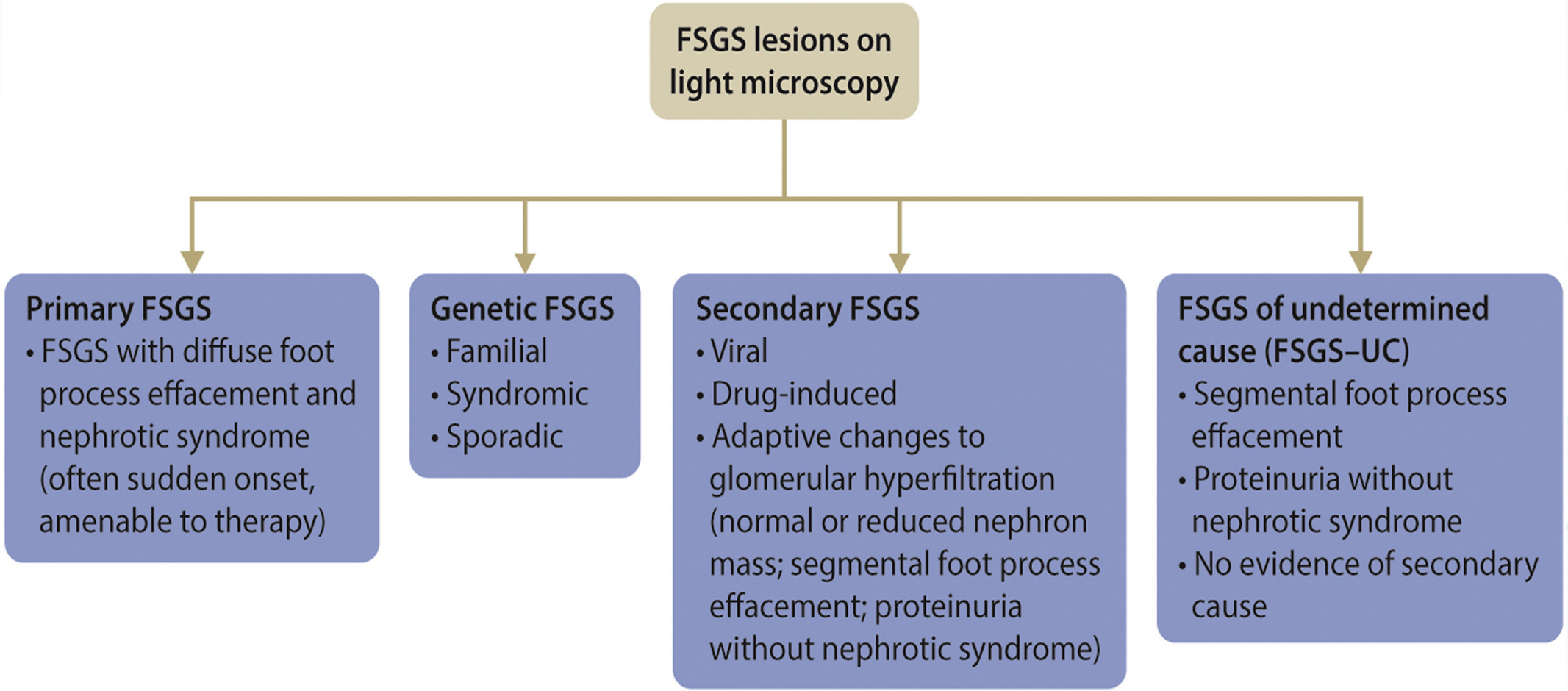
Recommendation 5.3.1: We recommend high-dose oral glucocorticoids for initial treatment of MCD (1C).

Practice Point 5.3.1: Algorithm for the initial treatment of MCD in adults

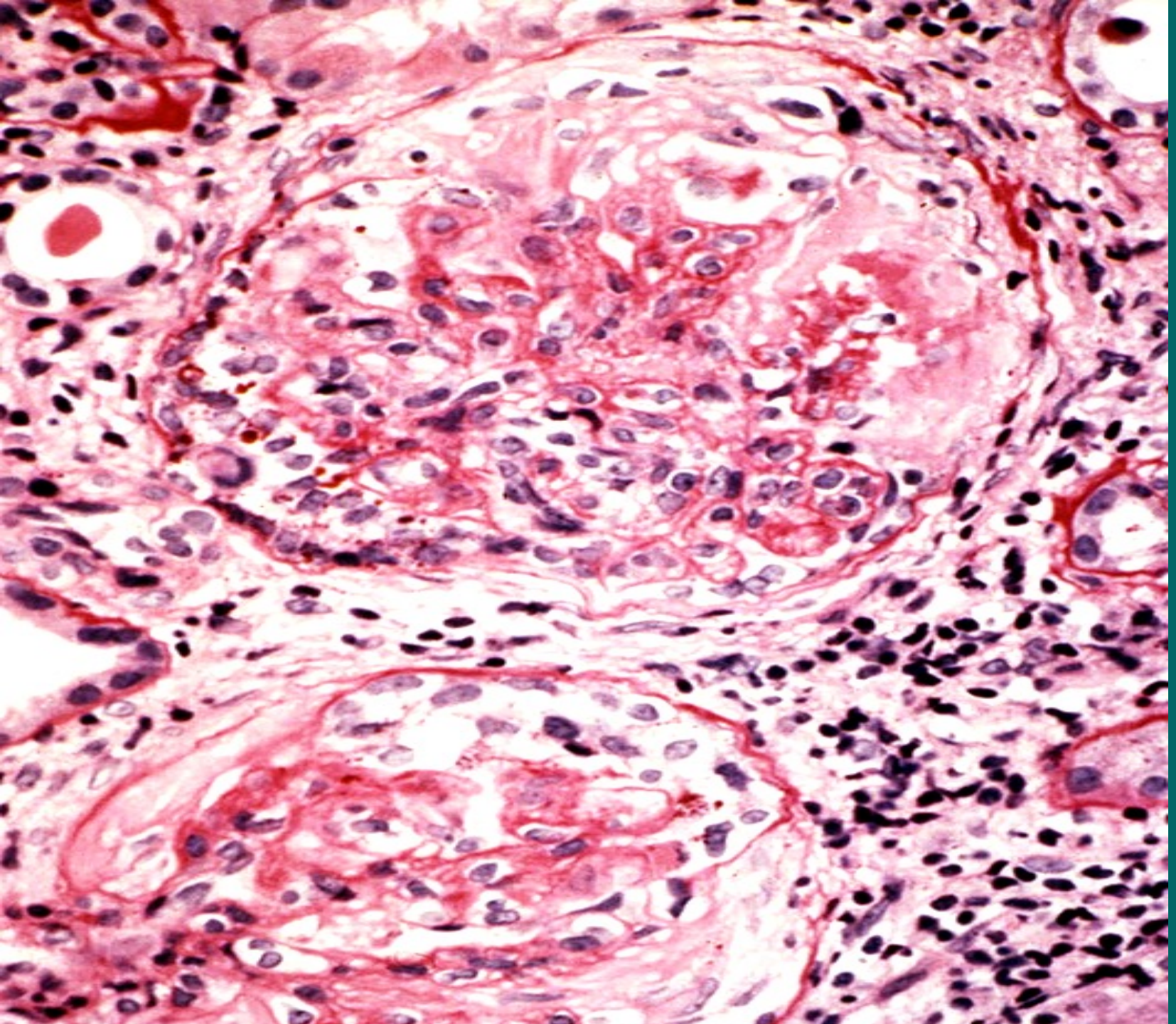


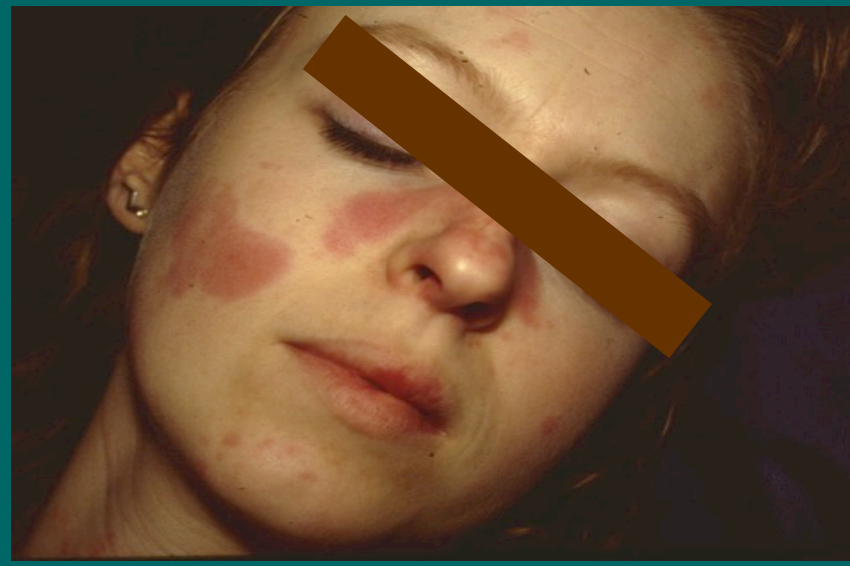
Practice Point 5.3.2: High-dose glucocorticoid treatment for MCD should be given for no longer than 16 weeks.

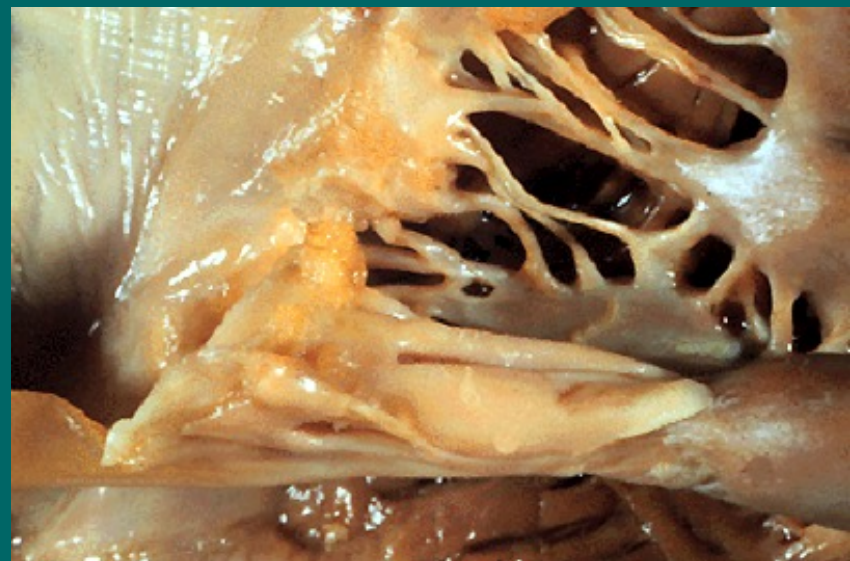
FSGS in Adults - Classification



LUPUS ERYTHEMATOSUS



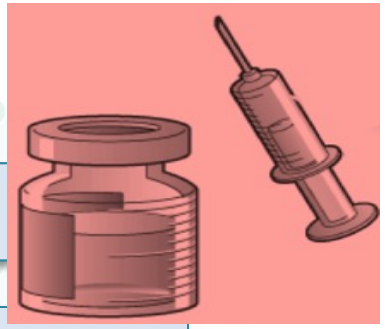




LUPUS NEPHRITIS

ISN/RPS classification	• does not consider tubulointerstitial injury, vascular lesions, or podocytopathies
Genetic testing	• no clear clinical benefits • risks & benefits of *APOL1* testing to be clarified
Repeat renal biopsy	• patients with clinical remission can still have histologic activity and vice versa
Prediction & Monitoring	• proteinuria at 1 year best predictor of long term renal outcome • biomarker panels will be required to accurately stratify risk, predict flare, determine + monitor treatment, and predict prognosis

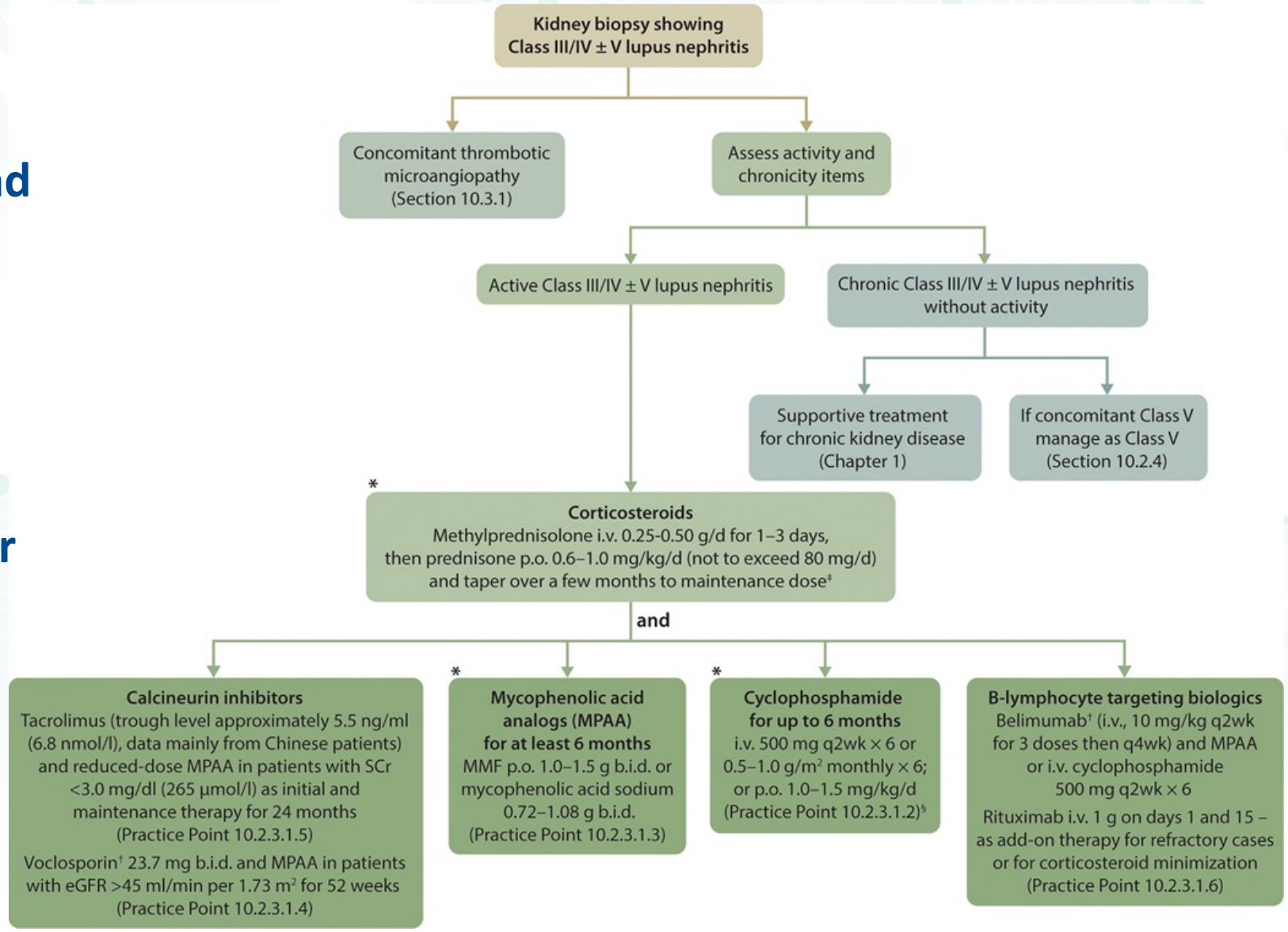
LUPUS NEPHRITIS



Antimalarials	• recommended for all patients with LN
Cortico-steroids	• use at lowest possible dose during maintenance • Low/zero-steroids protocols under investigation
CYC-/MMF-regimens	• remain the gold standard therapy for remission induction
Calcineurin-inhibitors	• Ongoing studies address role and toxicity in ethnically diverse populations
Maintenance Therapy	• minimum of 3 years, prolonged B-cell depletion with a RTX plus CYC may reduce the duration • A repeat kidney biopsy may be helpful

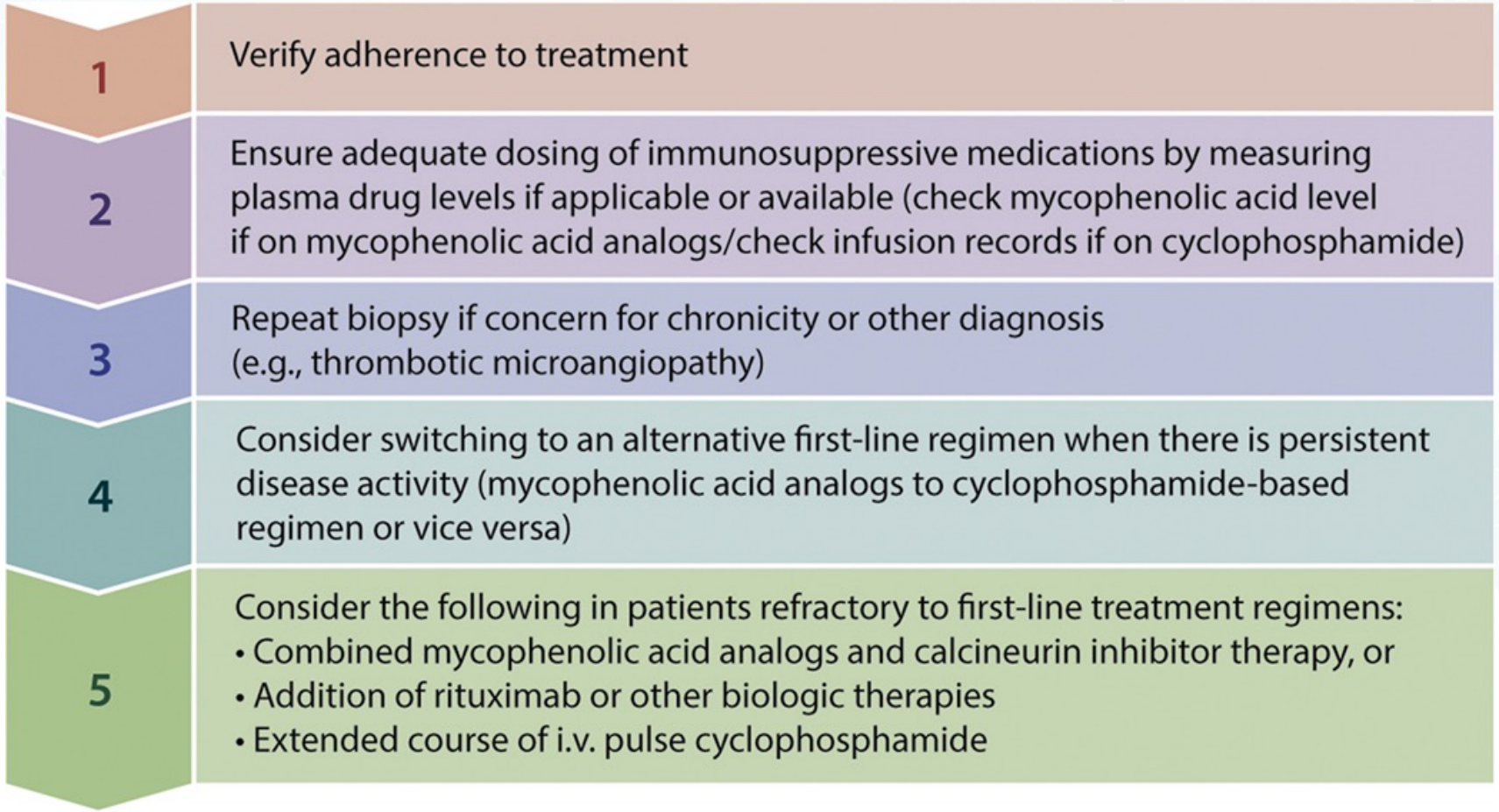
Lupus Nephritis – Treatment: Class III or Class IV LN: Initial therapy

Recommendation 10.2.3.1.1: We recommend that patients with active Class III or IV LN, with or without a membranous component, be treated initially with glucocorticoids plus either low-dose intravenous cyclophosphamide or MPAA (1B).

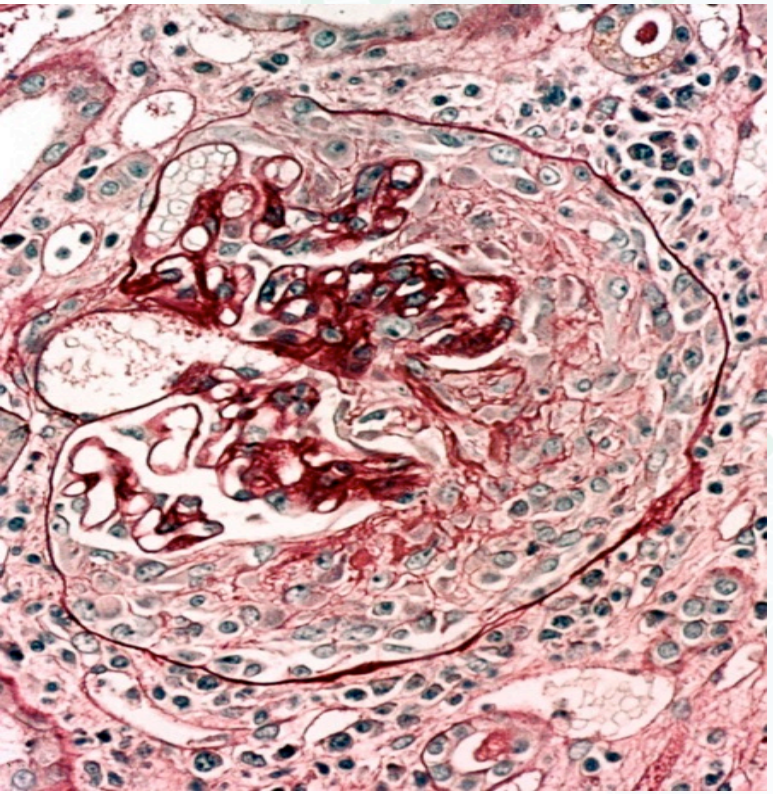


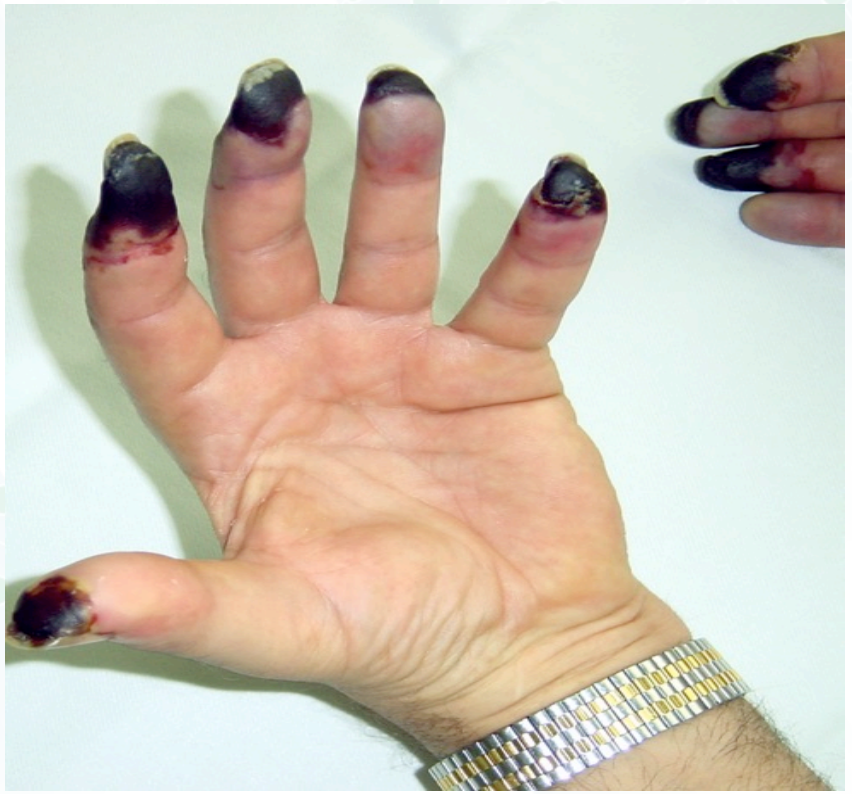
REFRACTORY LUPUS NEPHRITIS

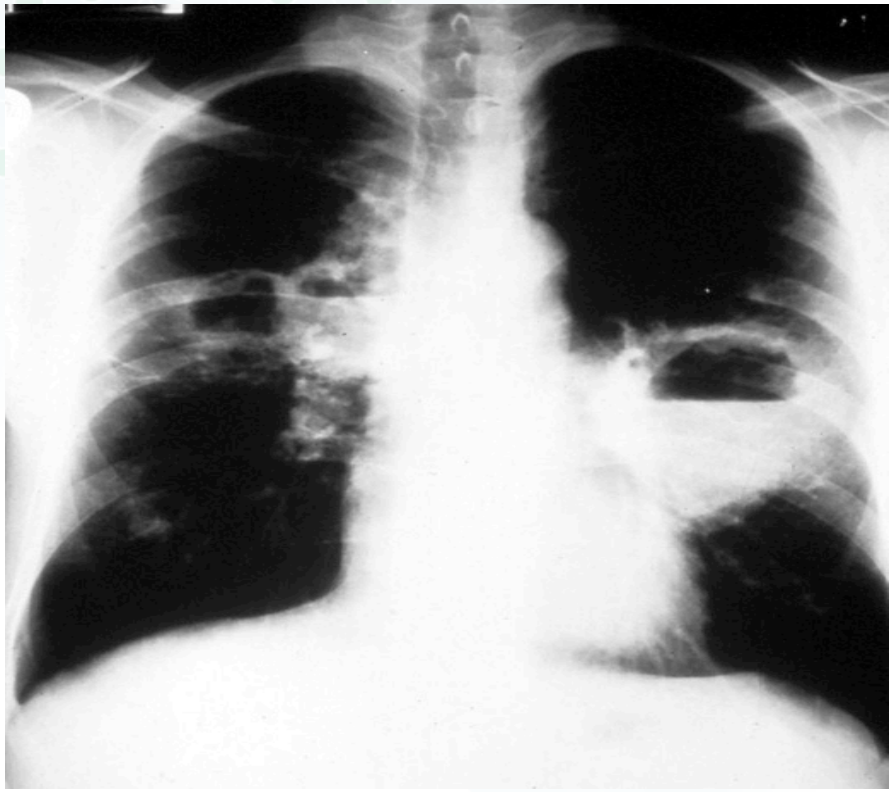
Practice Point 10.2.4.2.1: An algorithmic approach to patients whose response to therapy is deemed unsatisfactory is provided in the figure.



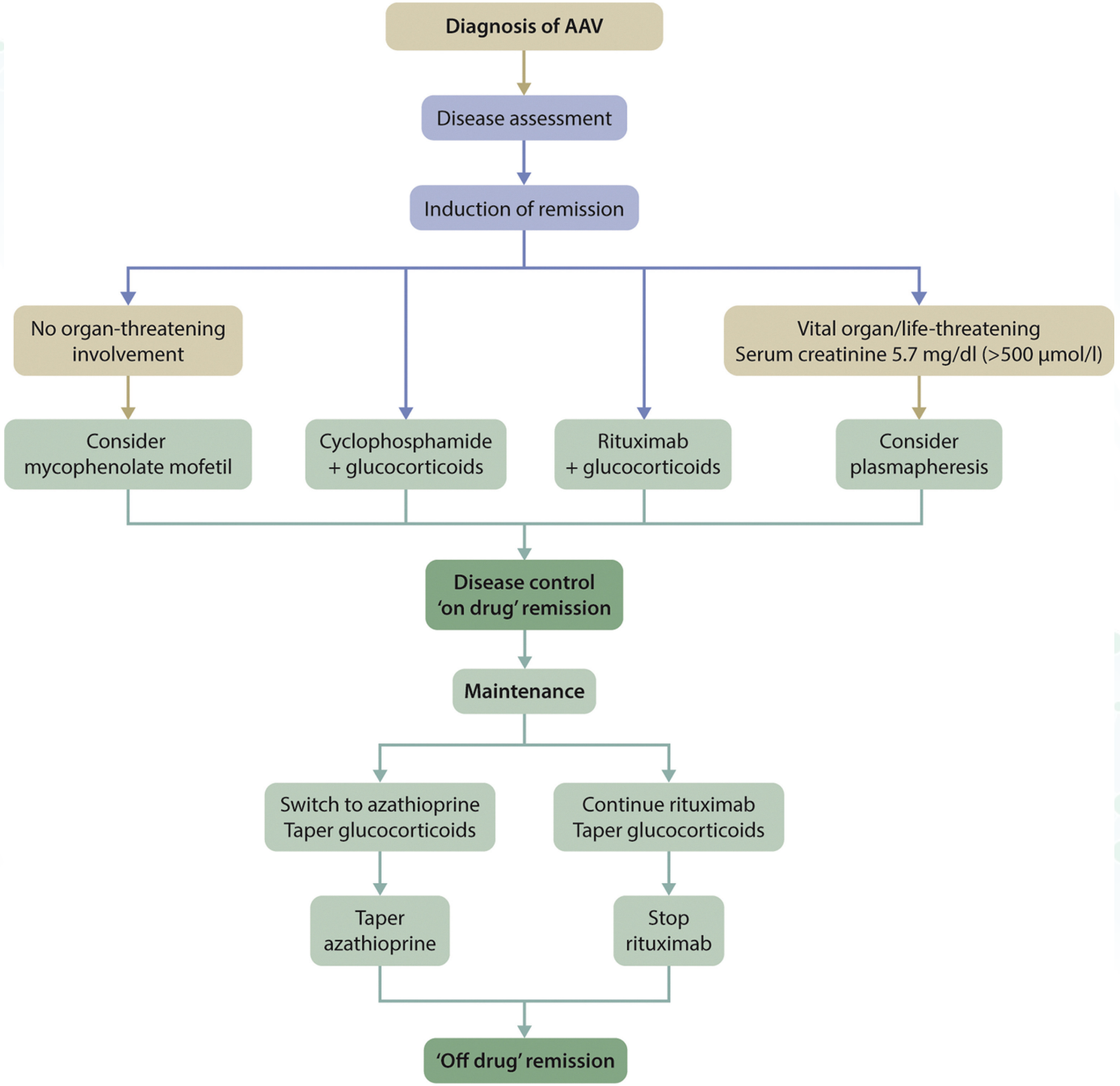
ANCA Vasculitis



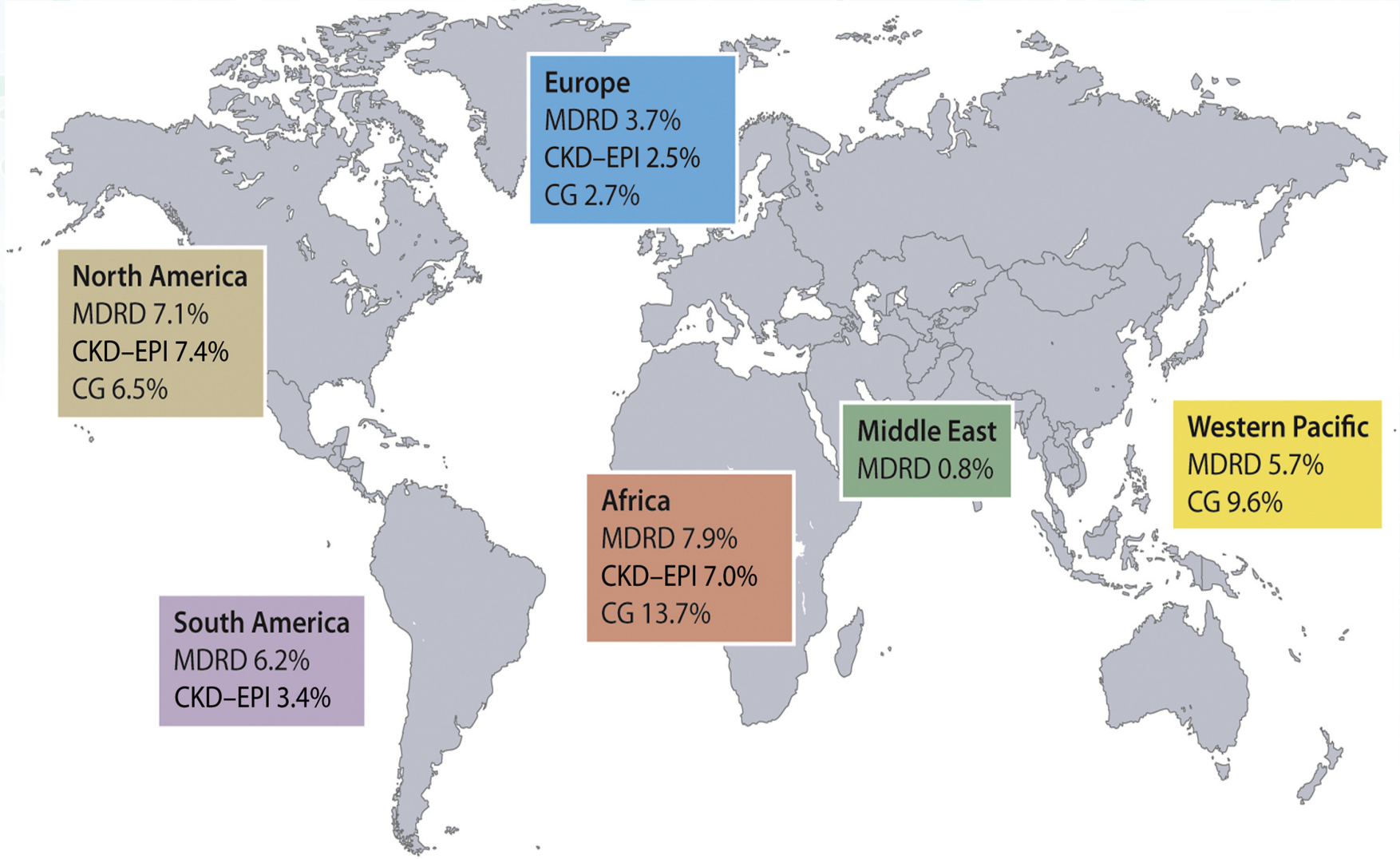




ANCA VASCULITIDES

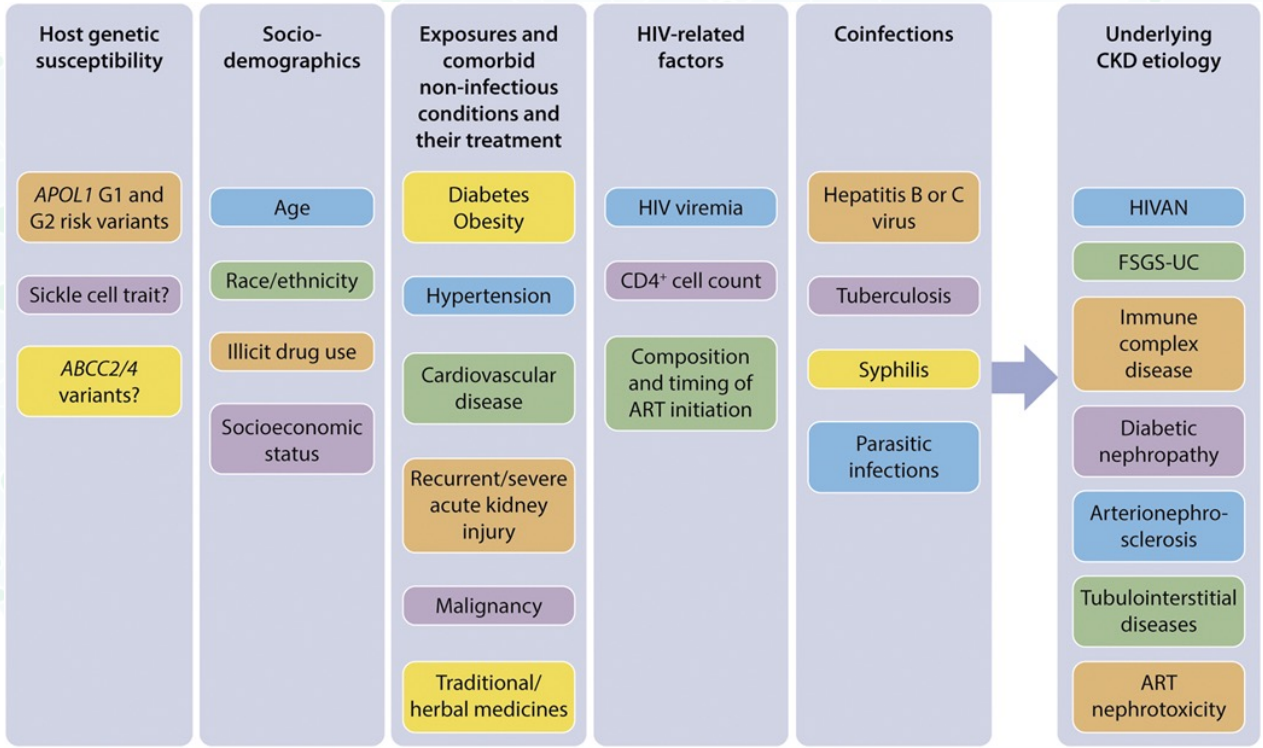


Viral Infection-related GN – Human Immunodeficiency virus (HIV)



Viral Infection-related GN – Human Immunodeficiency virus (HIV) - Prognosis

Practice Point 7.2.3.2.1: The factors contributing to the long-term outcome of HIV infection associated with GN are numerous and include persistence of viral replication, response to antiviral treatment, genetic predisposition to glomerular injury (e.g., APOL1 risk alleles), coinfection with other viruses, and development of immune complex disease or thrombotic microangiopathy. Thus, the estimation of prognosis in individual patients can be very difficult.



Viral Infection-related GN – Human Immunodeficiency virus (HIV) - Treatment

Recommendation 7.2.3.3.1: We recommend that antiretroviral therapy be initiated in all patients with HIV and CKD, especially biopsy-proven HIV-associated nephropathy (HIVAN), regardless of CD4 count, adjusted to the degree of kidney function (1C).

Practice Point 7.2.3.3.1: A decision for the use of glucocorticoids as an adjunct therapy for HIVAN must be made on a case-by-case basis, as the risks and benefits long-term are uncertain.

Nephropathies due to Infections – Schistosomal Nephropathy - Diagnosis

Practice Point 7.3.1.1.1: Test for appropriate endemic coinfections (Salmonella, HBV, HCV, HIV), as targeted treatment may alter the aggressiveness of an underlying GN or the sequela of schistosomiasis.

Practice Point 7.3.1.1.2: Obtain a kidney biopsy in patients suspected of having schistosomal GN in the presence of a viral coinfection (HCV, HBV, HIV).

AFRAN classification	Etiology
I Mesangial proliferative	*Schistosoma haematobium* *Schistosoma mansoni*
II Proliferative exudative	*Schistosoma haematobium* *Schistosoma mansoni* *Salmonella*
III Membranoproliferative	*Schistosoma haematobium* *Schistosoma mansoni*
IV Focal segmental glomerulosclerosis	*Schistosoma mansoni*
V Amyloidosis	*Schistosoma haematobium* *Schistosoma mansoni*
VI Cryoglobulinemia	*Schistosoma mansoni* Hepatitis C

Nephropathies due to Infections – Schistosomal Nephropathy - Treatment

Practice Point 7.3.1.2.1: Treat patients with schistosomal infection and GN with an appropriate antiparasitic agent in sufficient dosage and duration to eradicate the organism. There are no indications for use of immunosuppressive agents in schistosomal nephropathy.

Dosing	Praziquantel	Oxamniquine
Adult	20 mg/kg, 3 times a day, for 1 day	15 mg/kg, single dose
Pediatric >1 year old	20 mg/kg, 2–3 times a day, for 1 day	20 mg/kg, single dose

"Then, gentlemen, it is the consensus of this meeting that we say nothing, do nothing, and hope it all blows over before our next meeting."

Top 10 Takeaways for Clinicians from the KDIGO 2021 Clinical Practice Guideline for the Management of Membranous Nephropathy

1 Diagnosis of membranous nephropathy (MN)

A kidney biopsy is not required to diagnose membranous nephropathy in a patient with nephrotic syndrome and a positive PLA2Rab test, but may help in determining prognosis and treatment decisions. (Figure 1)

2 Added value of kidney biopsy staining

A negative PLA2Rab test does not rule out PLA2R-associated MN. PLA2Rab can be absent in early disease. A positive glomerular staining of a kidney biopsy for PLA2R defines PLA2R-associated MN.

3 Be aware of new antigens

Identification of new antigens might help in defining the underlying cause in PLA2Rab negative patients.

4 Exclude secondary causes of MN

Evaluate all patients with MN for secondary causes such as infections, systemic diseases, malignancies, certain drugs (NSAIDs) or nutritional supplements (lipoic acid).

5 Prophylactic anticoagulant therapy

Patients with MN are at high risk of arterial and venous thromboembolic events. Prophylactic anticoagulant therapy is advised in patients with low serum albumin levels taking into account bleeding risk. (Figure 2)

6 Conservative therapy

All patients should receive optimal supportive therapy targeting edema, blood pressure, dietary salt intake, and lipid profile. Monitor the patient regularly, whilst evaluating risk parameters (see below). The duration of conservative therapy might vary with risk levels and response.

7 Risk-based immunosuppressive therapy

Start of and the choice of immunosuppressive drugs are guided by risk evaluation based on a combination of change in serum creatinine, serum albumin, and proteinuria. (Figure 3) When available, serum PLA2Rab levels, urine protein selectivity index, and excretion of low molecular weight proteins provide added value.

8 Immunological monitoring

Whilst clinical remission is the goal of therapy, immunological response precedes clinical response by several months. In patients with PLA2Rab positive MN, regular assessment of PLA2Rab after start of therapy enables early evaluation of treatment response and provides guidance for treatment change.

9 Treatment resistance

Lack of clinical response after several lines of therapies defines resistance, and patients should be referred to an expert center to discuss additional therapy. Residual proteinuria per se is not a sign of active MN, and especially in patients with immunological remission or normalized serum albumin levels, secondary FSGS must be excluded.

10 Kidney transplantation

Evaluation of PLA2Rab and if necessary PLA2R-antigen aids in predicting post-transplant recurrence. In patients with recurrent MN and proteinuria >1 g/day rituximab is effective therapy. (Figure 4)

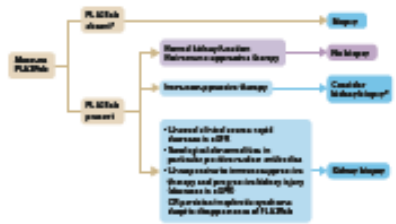


Figure 1

Figure 2

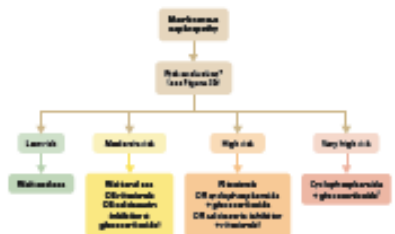


Figure 3

Figure 4

FSGS, focal segmental glomerulosclerosis; NSAIDS, nonsteroidal anti-inflammatory drugs; PLA2Rab, M-type phospholipase A2 receptor antibody

Top 10 Takeaways for Clinicians from the KDIGO 2021 Clinical Practice Guideline for the Management of ANCA-Associated Vasculitis (AAV)

1 Diagnosis of ANCA-associated vasculitis

Diagnosis of AAV must be made as early as possible to decrease the risk of permanent loss of kidney function and life-threatening complications. In case of clinical presentation compatible with small-vessel vasculitis in combination with positive myeloperoxidase (MPO)- or proteinase 3 (PR3)-ANCA serology, waiting for kidney biopsy should not delay starting immunosuppressive treatment, especially in patients who are rapidly deteriorating (Figure 1).

2 Initial treatment

Initial treatment of AAV is glucocorticoids in combination with cyclophosphamide or rituximab. In patients with markedly reduced or rapidly declining kidney function, cyclophosphamide is preferred because of limited experience with rituximab (Figure 2).

3 Rituximab as initial treatment

Rituximab is the preferred initial treatment in children and adolescents, pre-menopausal women and men concerned about their fertility, frail older adults, patients with relapsing disease, patients with PR3-ANCA disease and in patients in whom glucocorticoid-sparing is especially important.

4 Plasma exchange

Plasma exchange should be considered for patients with SCr >5.7 mg/dl (500 µmol/l) requiring dialysis or with rapidly increasing SCr, and in patients with diffuse alveolar hemorrhage who have hypoxemia (Figure 2). Plasma exchange should be added to initial treatment for patients with an overlap syndrome of ANCA vasculitis and anti-GBM.

5 Tapering of glucocorticoids

Although high-dose glucocorticoids have traditionally been given during the initial treatment of AAV, recent data demonstrated that lower doses are equally effective but with fewer short- and long-term toxicities.

6 Maintenance treatment

Maintenance therapy with either rituximab or azathioprine and low dose glucocorticoids is recommended after induction of remission (Figure 2). Optimal duration of the maintenance treatment is not known, but should be between 18 months and 4 years.

7 Preferred maintenance treatment

Rituximab as maintenance treatment is preferred in patients with relapsing disease, PR3-ANCA disease, frail older adults, azathioprine allergy, or when glucocorticoid-sparing is especially important.

8 Withdrawal of maintenance therapy

When considering withdrawal of maintenance therapy, the risk of relapse should be factored in, and patients should be informed of the need for prompt attention if symptoms recur.

9 Relapsing disease

Patients with relapsing disease (life- or organ-threatening) should be re-induced, preferably with rituximab.

10 Refractory disease

Patients with refractory disease can be treated by an increase in glucocorticoids (intravenous or oral), by the addition of rituximab if cyclophosphamide induction had been used previously, or vice versa. Plasma exchange can be considered.

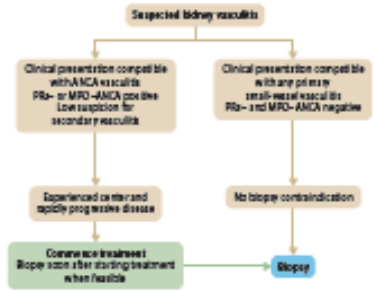


Figure 1

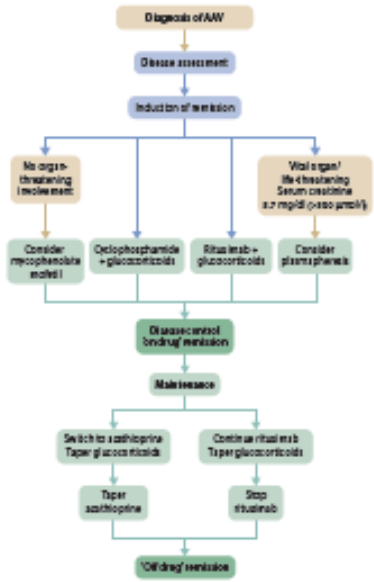


Figure 2

Guideline Updates

- Focused updating of specific chapters will be conducted based on new evidence
- The process will entail:
  - Conduct systematic searches for the topics of interest from 2020 to current date
  - Screen search results to identify new studies eligible for inclusion based on the inclusion criteria for the 2021 Update
  - Perform meta-analyses, where appropriate
  - WG will evaluate the change implications to the guideline recommendations and practice points based (wording, grading, need for additional statements) based on this new evidence review
  - Guideline text will be revised accordingly and presented to the full Work Group for consensus

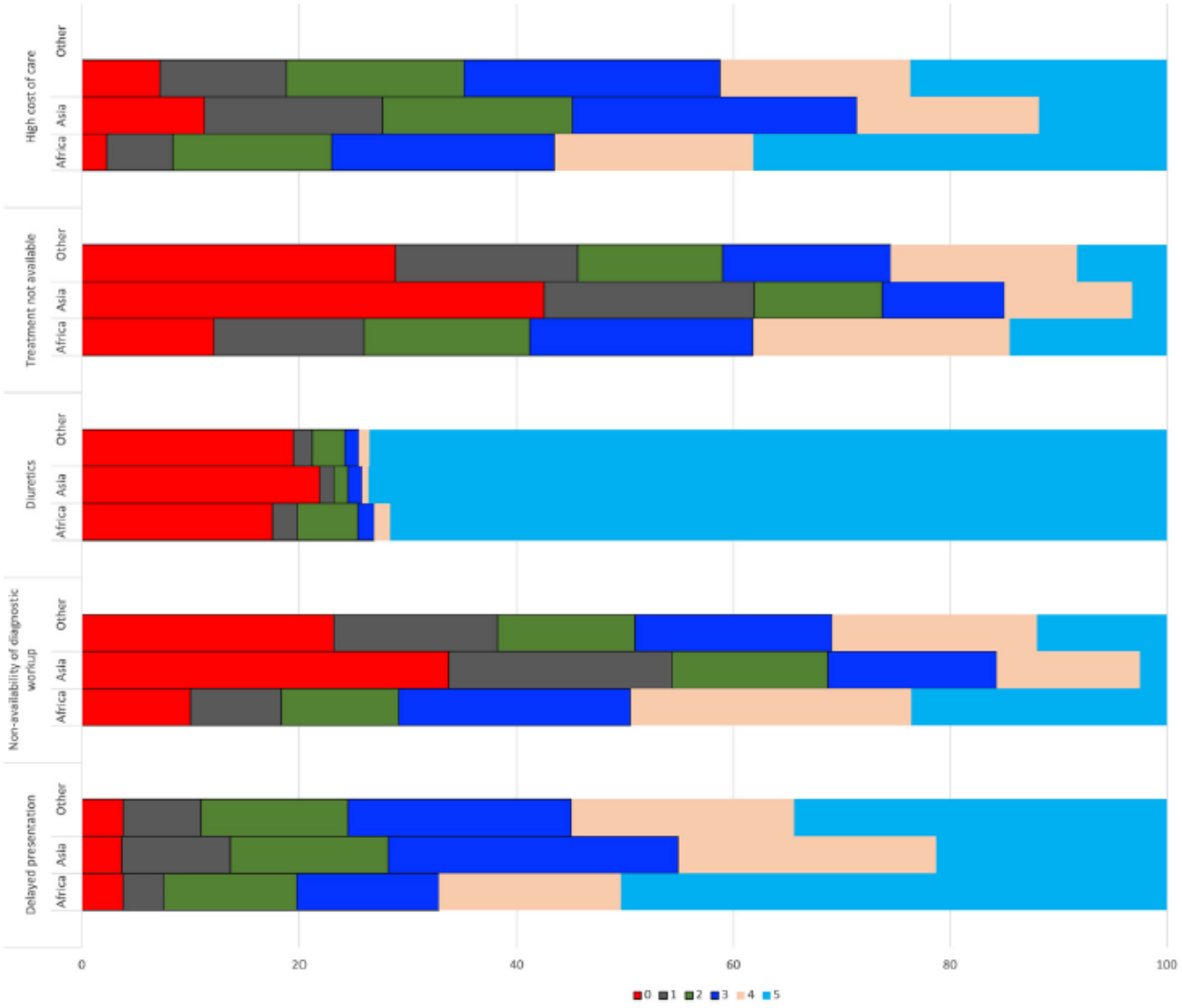
Challenges in Diagnosis and Management of Glomerular Disease in Resource-Limited Settings

High cost of care

Treatment not available

Diagnostic w/u not available

Delayed presentation



Ramachandran R,….Jha V. KI Reports 2022

"Good news.
Your cholesterol has stayed the same,
but the research findings have changed."