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The European Rare Kidney Disease Reference Network

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Working Group on Inherited Kidney Disorders

WELCOME TO

ERKNet
Advanced Webinars on Rare Kidney Disorders

Date: 29 June 2021

Topic: Update on KDIGO on immune glomerulopathies

Speaker: Jürgen Floege

Moderator: Jack Wetzels

The updated KDIGO Practice Guideline on Glomerular Diseases

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KDIGO Controversies Conference on Glomerular Diseases

Jürgen Floege - Conference Co-Chair
Brad Rovin - Conference Co-Chair

General Principles, MPGN, C3GN (Swallow Room)		IgAN (Galleria Ballroom)		Membranous GN (Falcon Room)		MCD & FSGS (Paradiso Room)		Lupus & ANCA (Cardinal Room)	
Breakout Group Co-Chairs									
Cattran (CA)	Dan	Barbour (CA)	Sean	Nachman (US)	Patrick	Gibson (US)	Keisha	Caster (US)	Dawn
Hogan (US)	Jonathan	Tang (HK)	Sydney	Wetzels (NL)	Jack	Moeller (DE)	Marcus	Roccatello (IT)	Dario

Key question: which of the 2012 guidelines for glomerulonephritis 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/m^2 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	
4.1.1: 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 SD SSNS 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 prednisone be given on alternate days in the lowest dose to maintain remission without major adverse effects in children with FR and SD SSNS. (*2D*)	✓
3.3.6: We suggest that rituximab be considered only in children with SD SSNS 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). (*2C*)	✓
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	
6.1.2: Do not routinely perform genetic testing. (*Not Graded*)	Refine
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 mycophenolate mofetil 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 20). (*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 5). (*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. (*2D*)	✗
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 (*2C*), or CNI (*2C*), 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 6–6.5 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. (*2D*)	✗
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 a rising 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*)	✓
active LN on biopsy with one of the alternative initial treatment regimens (see Section 12.3). (*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) involving the kidney in systemic lupus patients, with or without LN, be treated by anticoagulation (target international normalized ratio [INR] 2–3). (*2D*)	
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, ACE-I, 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. (*2D*)	
12.13 LN post-Transplant	Add statement in new guidelines

AAV	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 syndrome of ANCA vasculitis and anti-GBM GN, according to proposed criteria and regimen 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. (*2C*)	

Recommen-dations

(GRADE-Approach)*

Grade	Implications		
	Patients	**Clinicians**	**Policy**
Level 1 "We recommend"	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect lies close to that of the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of effect is very uncertain, and often will be far from the truth.

* Grading of Recommendations Assessment, Development and Evaluation

New Features: 2021 KDIGO clinical practice guideline on glomerular diseases

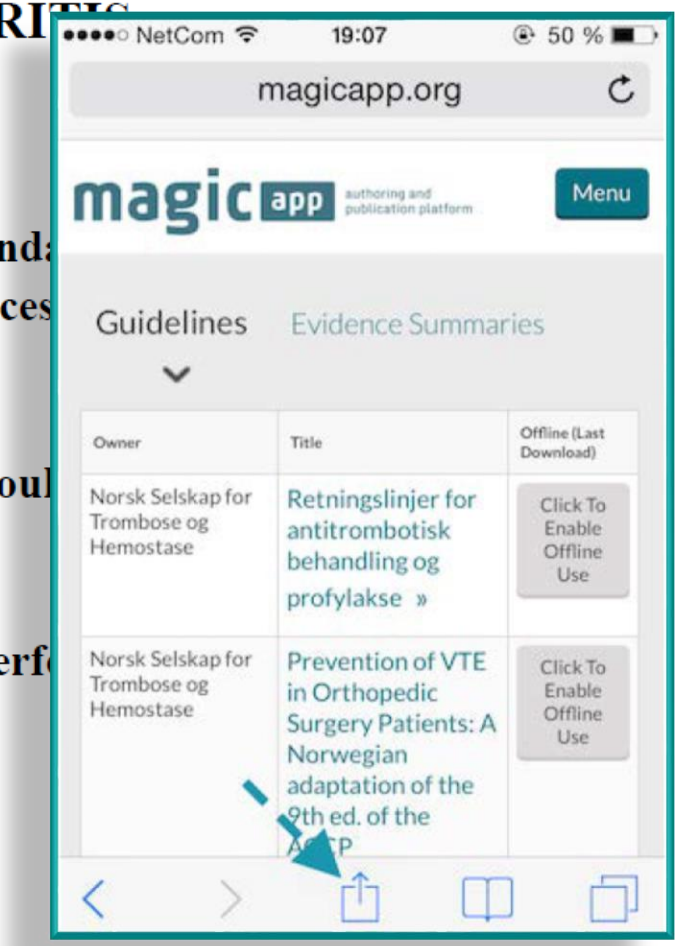
CHAPTER 1. GENERAL PRINCIPLES FOR THE MANAGEMENT OF GLOMERULONEPHRITIS

1.1. Kidney biopsy

Practice Point 1.1.1. The kidney biopsy is the "gold stand
glomerular diseases. However, under some circumstances
without a kidney biopsy confirmation of diagnosis.

Practice Point 1.1.2. The evaluation of kidney tissue shoul
adequacy.

Practice Point 1.1.3. Repeat kidney biopsy should be perf
potentially alter the therapeutic plan.



2021 KDIGO Management of Glomerular Diseases

www.kidney-international.org

KDIGO executive conclusions

Executive summary of the KDIGO 2021 Guideline for the Management of Glomerular Diseases

Check for updates

OPEN

Brad H. Rovin[1], Sharon G. Adler[2], Jonathan Barratt[3], Frank Bridoux[4], Kelly A. Burdge[5], Tak Mao Chan[6], H. Terence Cook[7], Fernando C. Fervenza[8], Keisha Gibson[9], Richard J. Glassock[10], David Jayne[11], Vivekanand Jha[12,13,14], Adrian Liew[15], Zhi-Hong Liu[16], Juan M. Mejia-Vilet[17], Carla M. Nester[18], Jai Radhakrishnan[19], Elizabeth M. Rave[20], Heather N. Reich[21], Pierre Ronco[22], Jan-Stephan Sanders[23], Sanjeev Sethi[8], Yusuke Suzuki[24], Sydney C.W. Tang[6], Vladimir Tesar[25], Marina Vivarelli[26], Jack F.M. Wetzels[27], Lyubov Lytvyn[28], Jonathan C. Craig[29,30], David J. Tunnicliffe[30,31], Martin Howell[30,31], Marcello Tonelli[32], Michael Cheung[33], Amy Earley[33] and Jürgen Floege[34]

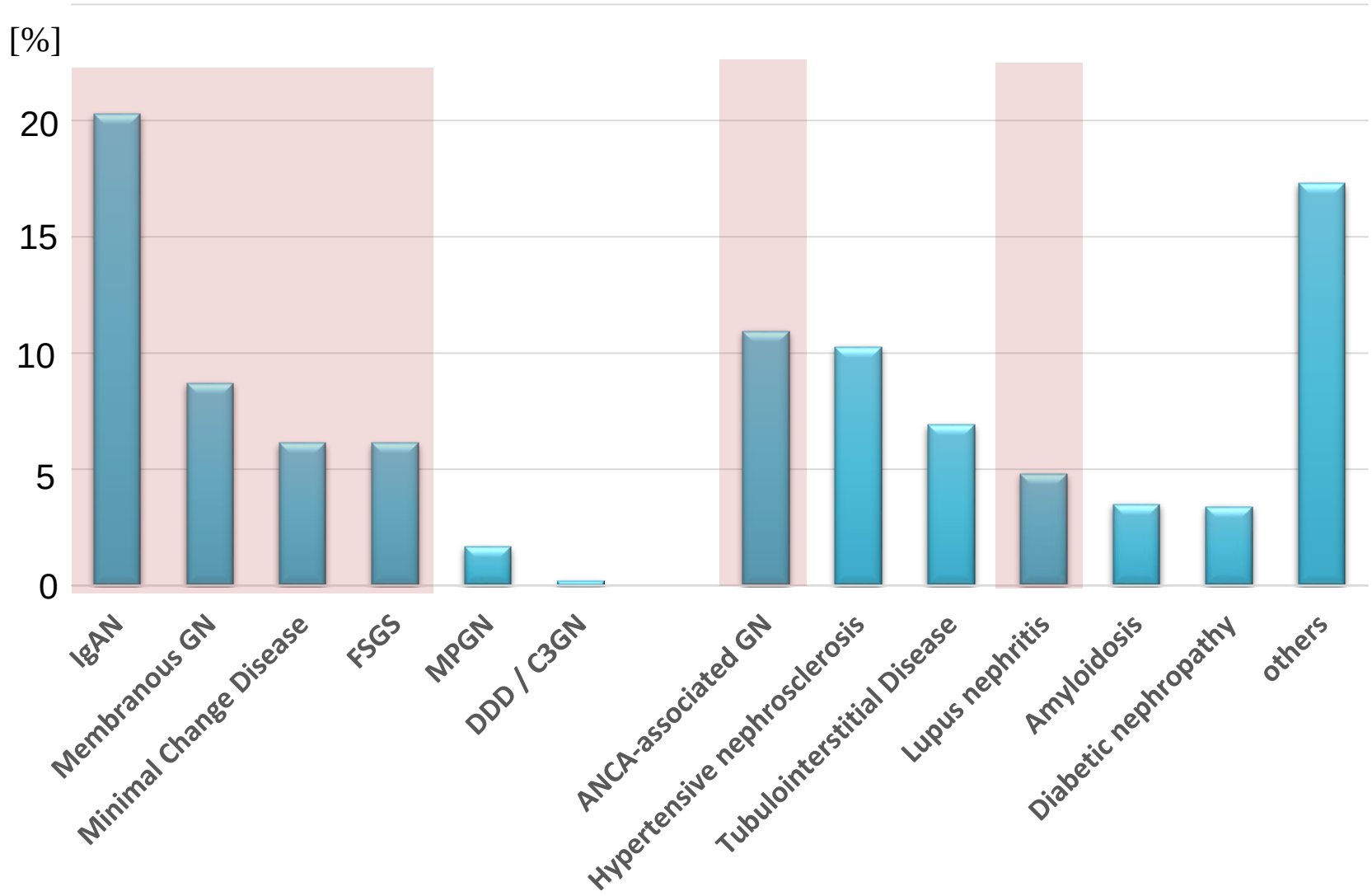
Oktober 2021 in press

KDIGO 2021 Guideline for the Management of Glomerular Diseases

- Summary of recommendation statements and practice points
- Chapter 1. General principles for the management of glomerular disease
- Chapter 2. Immunoglobulin A nephropathy/Immunoglobulin A vasculitis
- Chapter 3. Membranous nephropathy
- Chapter 4. Nephrotic syndrome in children
- Chapter 5. Minimal change disease in adults
- Chapter 6. Focal segmental glomerulosclerosis in adults
- Chapter 7. Infection-related glomerulonephritis
- Chapter 8. Immunoglobulin and complement-mediated glomerular diseases with an membranoproliferative glomerulonephritis (MPGN) pattern of injury.
- Chapter 9. ANCA-associated vasculitis
- Chapter 10. Lupus nephritis
- Chapter 11. Anti-GBM antibody glomerulonephritis

Floege & Amann, Lancet 2016

Glomerulonephritis-Types encountered in Europe



Kidney biopsy diagnoses in 2243 adult patients undergoing native kidney biopsy at the Division of Nephrology, Aachen University Hospital between 1990 and 2013.

IgA nephropathy

<u>2.2. Prognosis</u> Practice Point 2.2.1. Considerations for the prognostication of primary IgAN:

- **Clinical and histologic data at the time of biopsy can be used to risk assess the patient using the International IgAN Prediction Tool available at QxMD.**
- **The International IgAN Prediction Tool cannot be used to determine the likely impact of any particular treatment regimen.**
- **There are no validated *<u>prognostic</u>* serum or urine biomarkers for IgAN.**

Research

JAMA Internal Medicine | Original Investigation

Evaluating a New International Risk-Prediction Tool in IgA Nephropathy

Sean J. Barbour, MD, MSc; Rosanna Coppo, MD, FERA; Hong Zhang, MD, PhD; Zhi-Hong Liu, MD; Yusuke Suzuki, MD, PhD; Keiichi Matsuzaki, MD, PhD; Ritsuko Katafuchi, MD, PhD; Lee Er, MSc; Gabriela Espino-Hernandez, MSc; S. Joseph Kim, MD, PhD; Heather N. Reich, MD, PhD; John Feehally, FRCP; Daniel C. Cattran, MD, FRCPC; for the International IgA Nephropathy Network

IgA nephropathy

Practice Point 2.3.1. Considerations for treatment of all patients with IgAN

- **The primary focus of management should be optimized supportive care.**
- **Assess cardiovascular risk and commence appropriate interventions as necessary.**
- **Give lifestyle advice including information on dietary sodium restriction, smoking cessation, weight control, and exercise as appropriate.**

Level 1 Recommendations

- Control blood pressure (sitting systol. BP in the 120s)
- ACEI or ARB therapy (uptitrate + maybe combine)
- Avoid dihydropyridine type calciumchannel-blockers
- Control protein intake

ALL

Level 2 Recommendations

- Restrict NaCl- and fluid-intake, diuretics
- Non-dihydropyridine type calciumchannel-blockers
- Control all components of the metabolic syndrome
- Aldosterone antagonist, ß-blocker
- Stop smoking
- Low evidence: $NaHCO_3$ therapy, independent of metabolic acidosis

As many measures as possible

Floege & Eitner, JASN 2011

Floege & Feehally Nat Rev Nephrol 2013

IgA nephropathy

Recommendation 2.3.2.
We recommend that all patients with proteinuria >0.5 g/24h, irrespective of whether they have hypertension, are treated with either an ACEi or ARB *(1B)*.

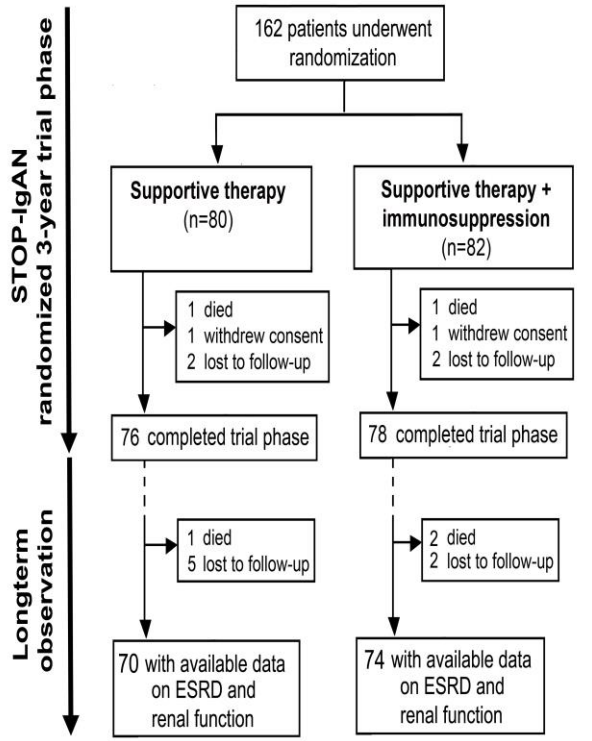
Recommendation 2.3.3.
We suggest that patients who remain at high risk of progressive CKD despite maximal supportive care are considered for a six-month course of corticosteroid therapy.
The important risk of treatment-emergent toxicity must be discussed with patients, particularly those who have an eGFR below 50 ml/min/1.73 m2 (2B).

Use extreme caution or avoided entirely if:
eGFR < 30 mL/min/1.73 m^2 *
Diabetes
Obesity (BMI > 30 kg/m^2) **
Latent infections (e.g. hepatitis, TB)
Secondary disease (e.g. cirrhosis)
Active peptic ulceration
Uncontrolled psychiatric illness

STOP-IgAN trial: Long-term Renal Outcomes

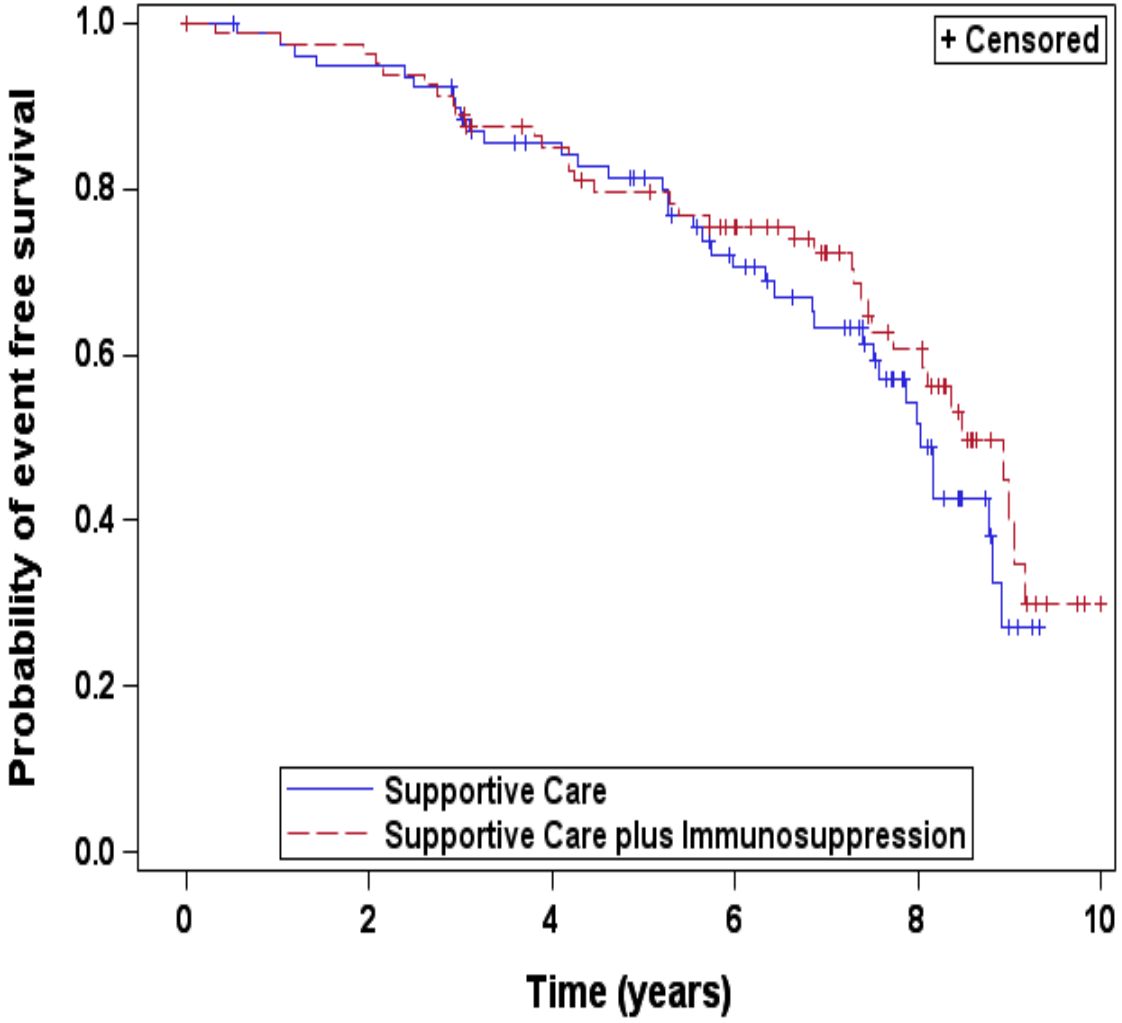
Long-term

92% with longterm follow-up (median 7.4 yrs)



Pts. with available EP information (i.e. death, ESRD and eGFR-loss >40%) at end of longterm observation	72 (90.0%)	77 (93.9%)

Long-term endpoint (death, ESRD or eGFR-loss >40%)



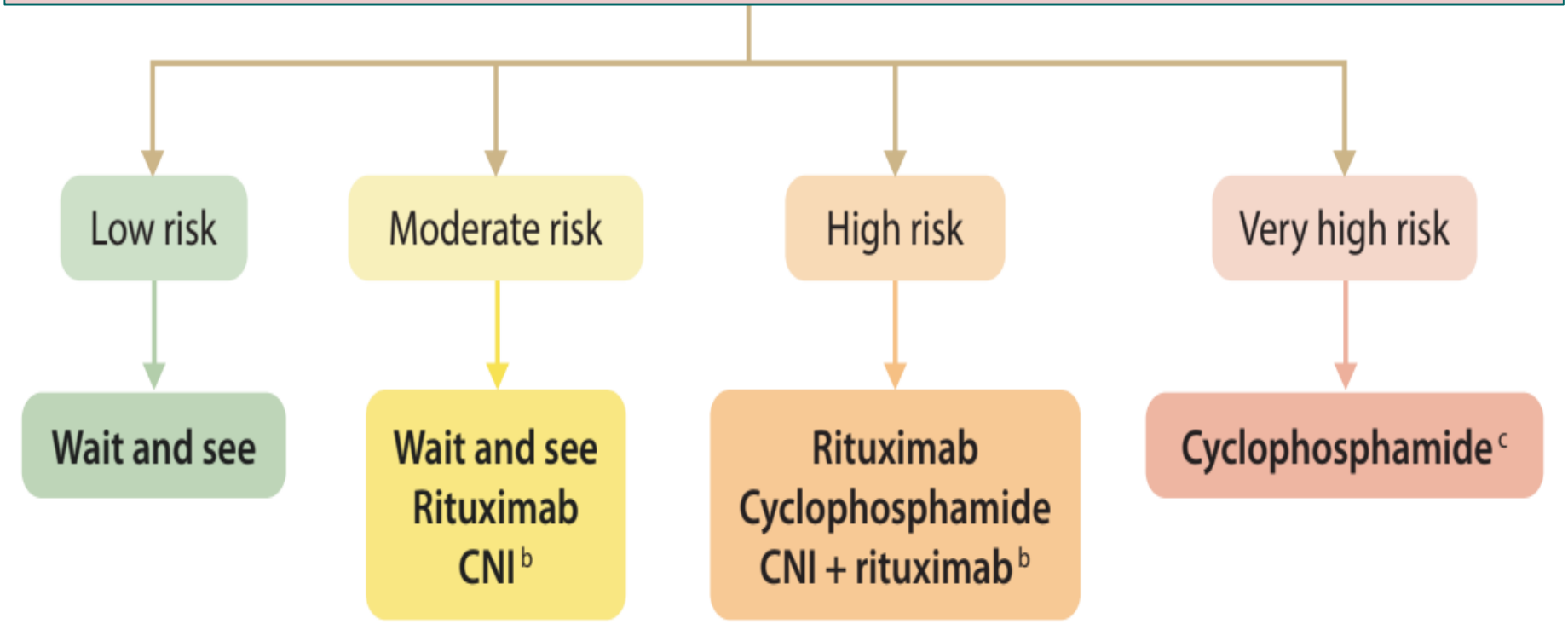
Membranous nephropathy

Practice Point 3.2.1. In patients with MN, use clinical and laboratory criteria to assess the risk of progressive loss of kidney function

Low risk	Moderate risk	High risk	Very high risk
• Normal eGFR, proteinuria < 3.5 g/day and/or serum albumin > 30 g/L	• Normal eGFR, proteinuria > 4 g/day and no decrease > 50% after 6 months of conservative therapy with ACE/ARB • PLA2Rab < 50 RU/ml [b] • Mild LMW proteinuria • Selectivity index < 0.15 • U IgG < 250 mg/day	• eGFR < 60 ml/min/1.73 m^2 [a] • Proteinuria > 8 g/day for > 6 months • PLA2Rab > 150RU/ml [b] • High LMW proteinuria • U IgG > 250 mg/day • Selectivity index > 0.20	• Life-threatening nephrotic syndrome • Rapid deterioration of kidney function not otherwise explained • High LMW proteinuria in two urine samples collected with interval of 6–12 months

Membranous nephropathy

Recommendation 3.3.1.
For patients with MN and at least one risk factor for disease progression, we recommend using rituximab, or cyclophosphamide and steroids for six months, or tacrolimus-based therapy for at least six months, with the choice of treatment depending on the risk estimate (1B).



MENTOR: Rituximab vs. CyA bei membranöser GN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rituximab or Cyclosporine in the Treatment of Membranous Nephropathy

1 g on d1+d14

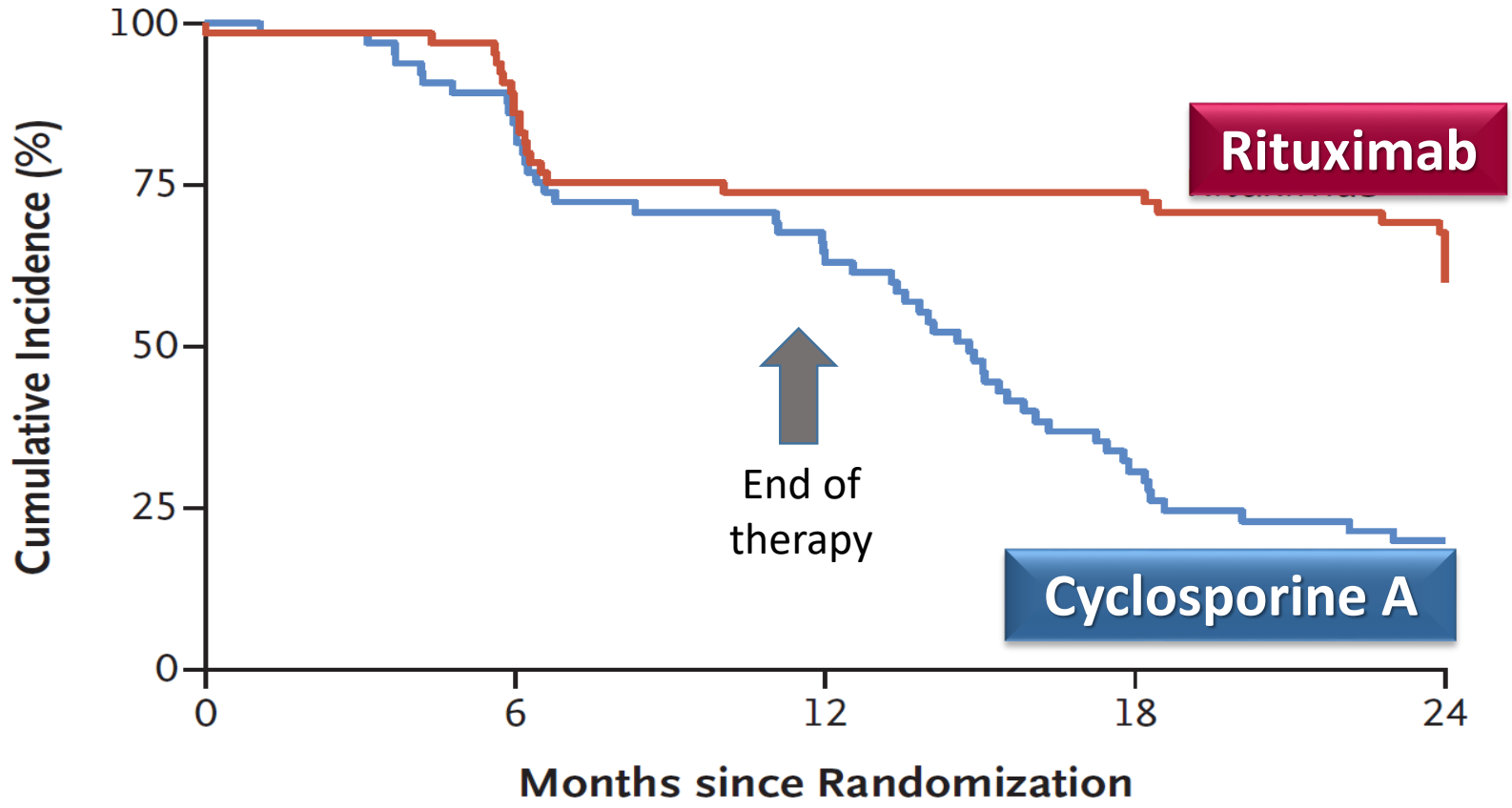
F.C. Fervenza, G.B. Appel, S.J. Barbour, B.H. Rovin, R.A. Lafayette, N. Aslam, J.A. Jefferson, P.E. Gipson, D.V. Rizk, J.R. Sedor, J.F. Simon, E.T. McCarthy, P. Brenchley, S. Sethi, C. Avila-Casado, H. Beanlands, J.C. Lieske, D. Philibert, T. Li, L.F. Thomas, D.F. Green, L.A. Juncos, L. Beara-Lasic, S.S. Blumenthal, A.N. Sussman, S.B. Erickson, M. Hladunewich, P.A. Canetta, L.A. Hebert, N. Leung, J. Radhakrishnan, H.N. Reich, S.V. Parikh, D.S. Gipson, D.K. Lee, B.R. da Costa, P. Jüni, and D.C. Cattran, for the MENTOR Investigators

N Engl J Med 2019;381:36-46.

Fervenza FC et al, N Engl J Med 2019; 381: 36-46

MENTOR: Rituximab vs. CyA in membranous GN

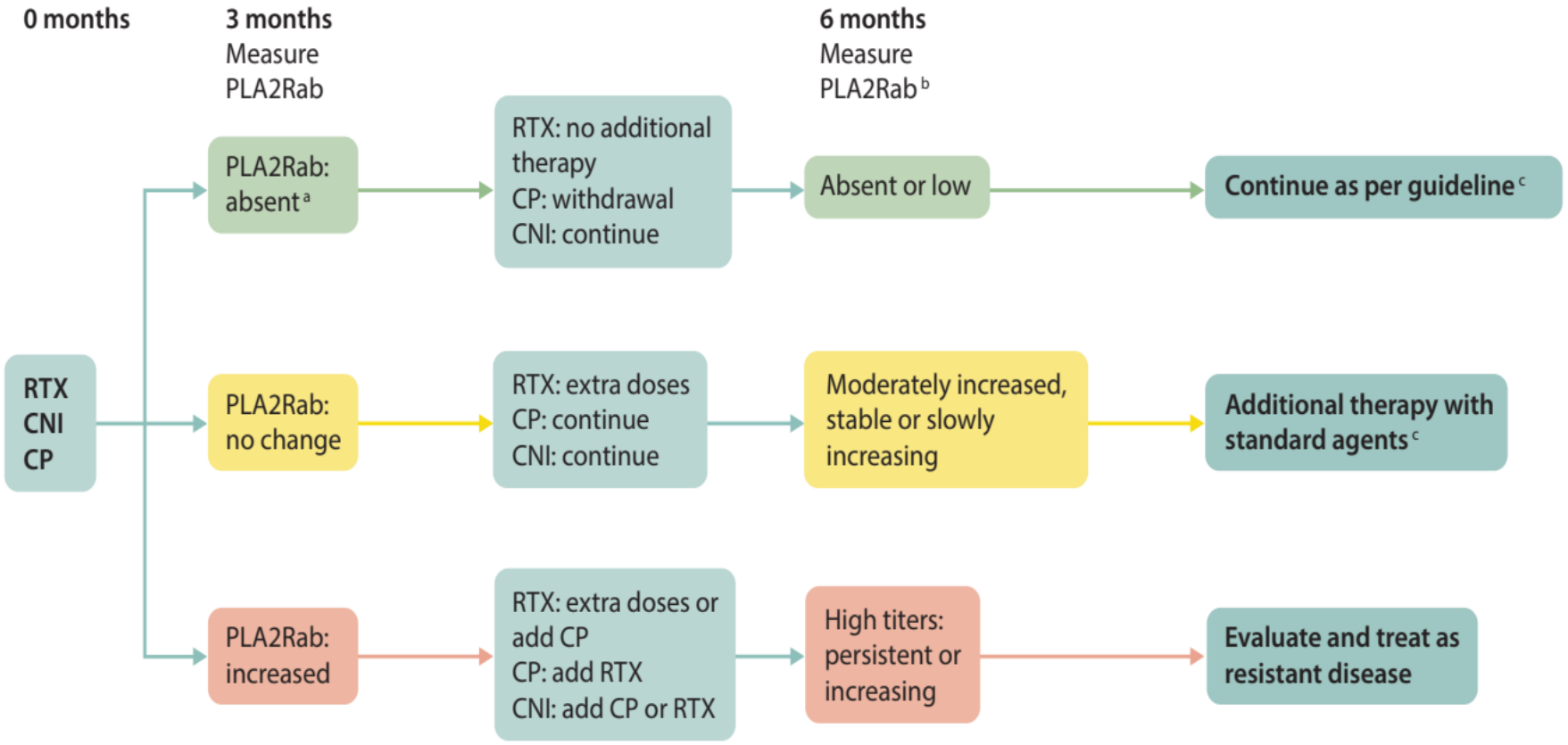
Partial or full remission at 24 months



No. at Risk					
Rituximab	65	59	48	48	44
Cyclosporine	65	56	42	20	13

Membranous nephropathy

Practice Point 3.3.3. Longitudinal monitoring of PLA2Rab levels at three and six months after start of therapy may be useful for evaluating treatment response in patients with membranous nephropathy, and can be used to guide adjustments to therapy



Nephrotic syndrome in children

Recommendation 4.3.1.1: **We recommend that oral glucocorticoids be given for 8 weeks** (4 weeks of daily glucocorticoids followed by 4 weeks of alternate-day glucocorticoids) **or 12 weeks** (6 weeks of daily glucocorticoids followed by 6 weeks of alternate-day glucocorticoids) **(1B).**

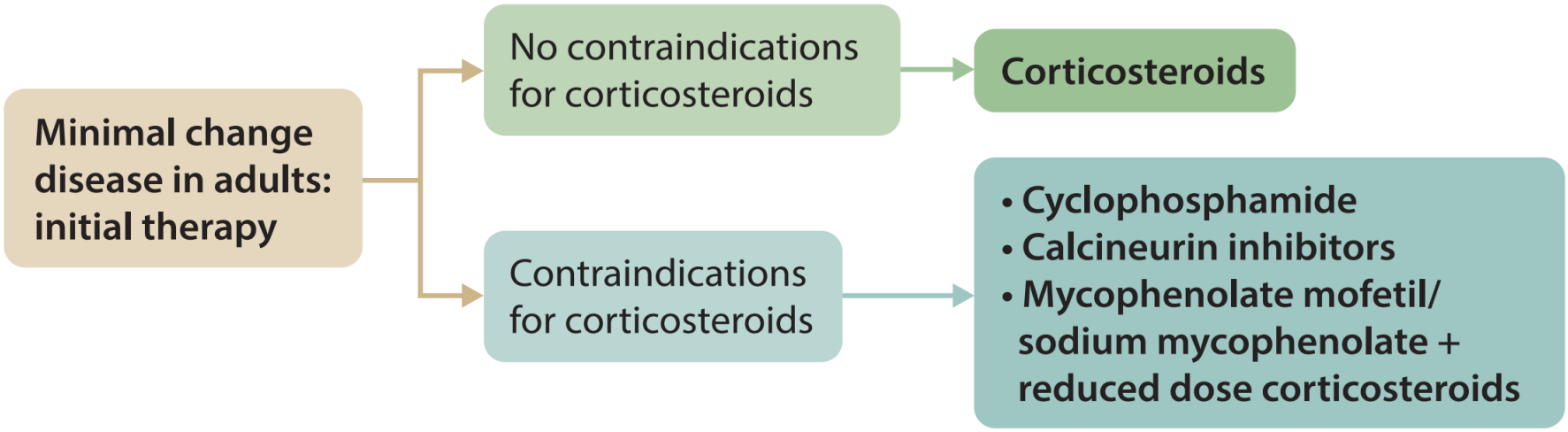
Recommendation 4.3.2.1: **For children with frequently relapsing and steroid-dependent nephrotic syndrome who are currently taking alternate-day glucocorticoids or are off glucocorticoids, we recommend that daily glucocorticoids 0.5 mg/kg be given during episodes of upper respiratory tract and other infections for 5–7 days to reduce the risk of relapse (1C).**

Recommendation 4.3.2.2: **For children with frequently relapsing nephrotic syndrome who develop serious glucocorticoid-related adverse effects and for all children with steroid-dependent nephrotic syndrome, we recommend that glucocorticoid-sparing agents* be prescribed, rather than no treatment or continuation with glucocorticoid treatment alone (1B).**

* oral cyclophosphamide, levamisole, mycophenolate mofetil (MMF), rituximab, or calcineurin inhibitors (CNIs).

Minimal Change Disease in adults

Recommendation 5.3.1. We recommend high dose oral corticosteroids for initial treatment of MCD *(1C)*.



Recommendation 5.3.1.1. We suggest cyclophosphamide, rituximab, calcineurin inhibitors, or mycophenolic acid analogs (MPAA) for the treatment of frequently-relapsing/corticosteroid-dependent MCD as compared to prednisone alone or to no treatment (1C).

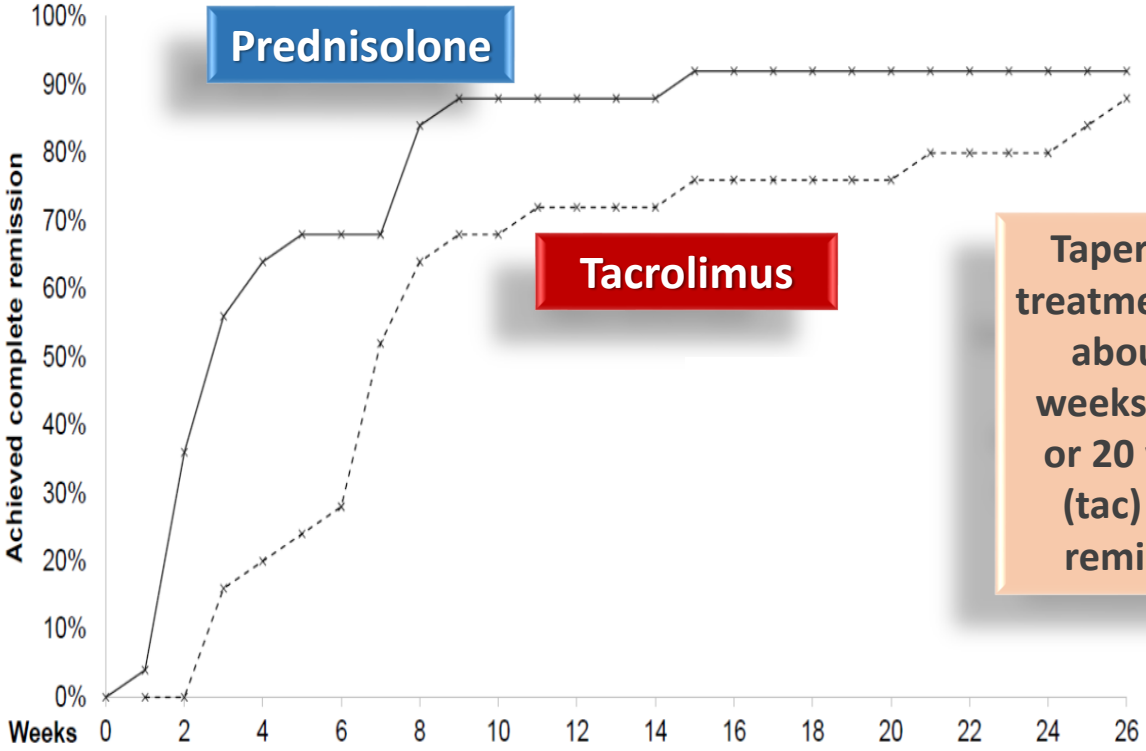
Medjeral-Thomas NR et al, CJASN 15: 209–218, 2020

Minimal Change

Tacrolimus versus corticosteroid monotherapy for adult minimal change nephropathy

British multicenter trial, median eGFR about 100 ml/min, median proteinuria about 7 g/d
Tacrolimus 0.05 mg/kg twice daily (N=25) vs. prednisolone starting at 1 mg/kg/d (N=25)

Primary end point:
Achievement of complete remission at week 8



Weeks	0	2	4	6	8	10	12	14	16	18	20	22	24	26
Prednisolone	0	9	16	17	21	22	22	22	23	23	23	23	23	23
Tacrolimus	0	4	6	13	17	18	18	19	19	19	20	20	21	22

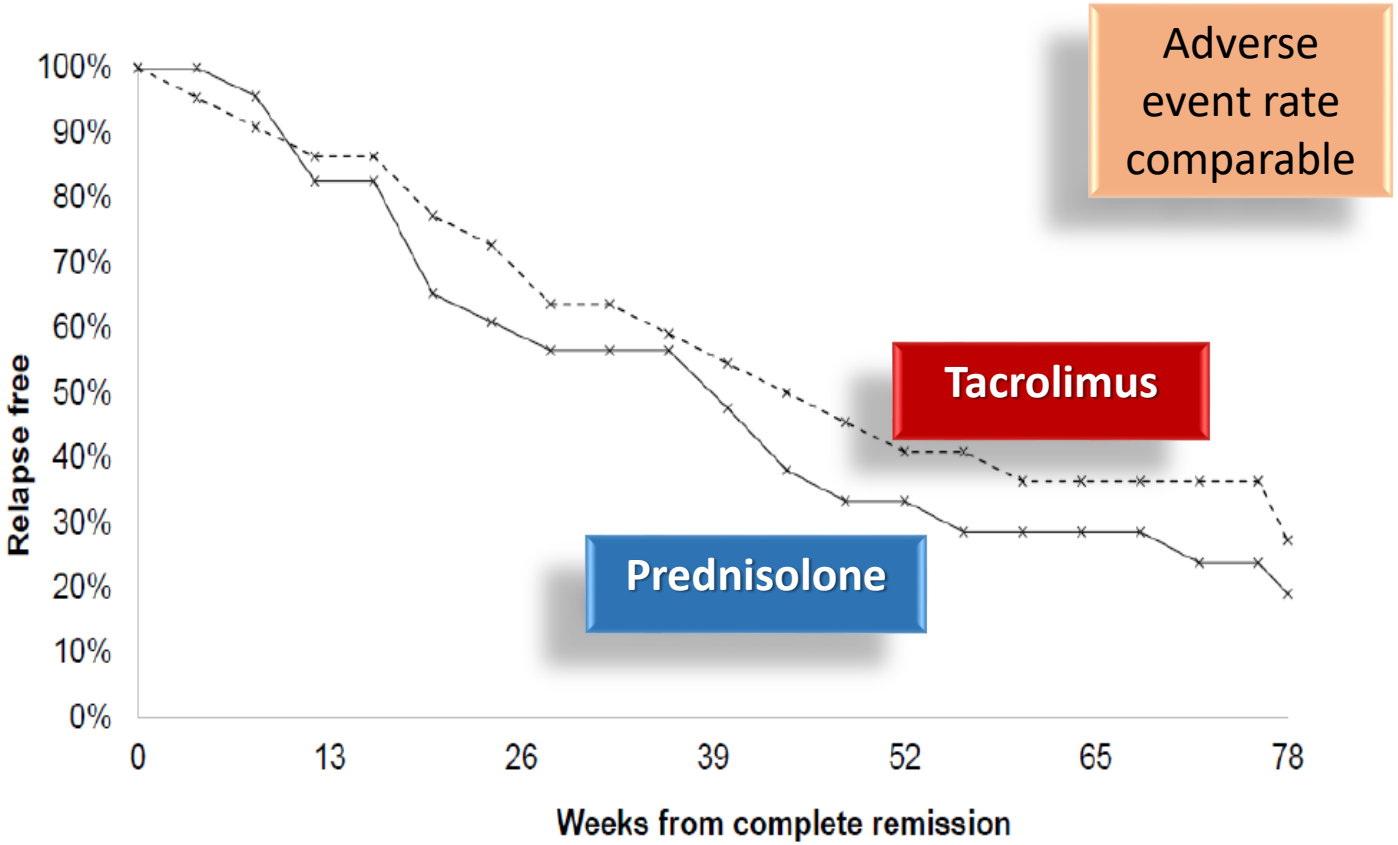
Tapering of treatment over about 12 weeks (pred) or 20 weeks (tac) after remission

Medjeral-Thomas NR et al, CJASN 15: 209–218, 2020

Tacrolimus versus corticosteroid monotherapy for adult minimal change nephropathy

Secondary end point:

Relapse rate in those who achieved full remission



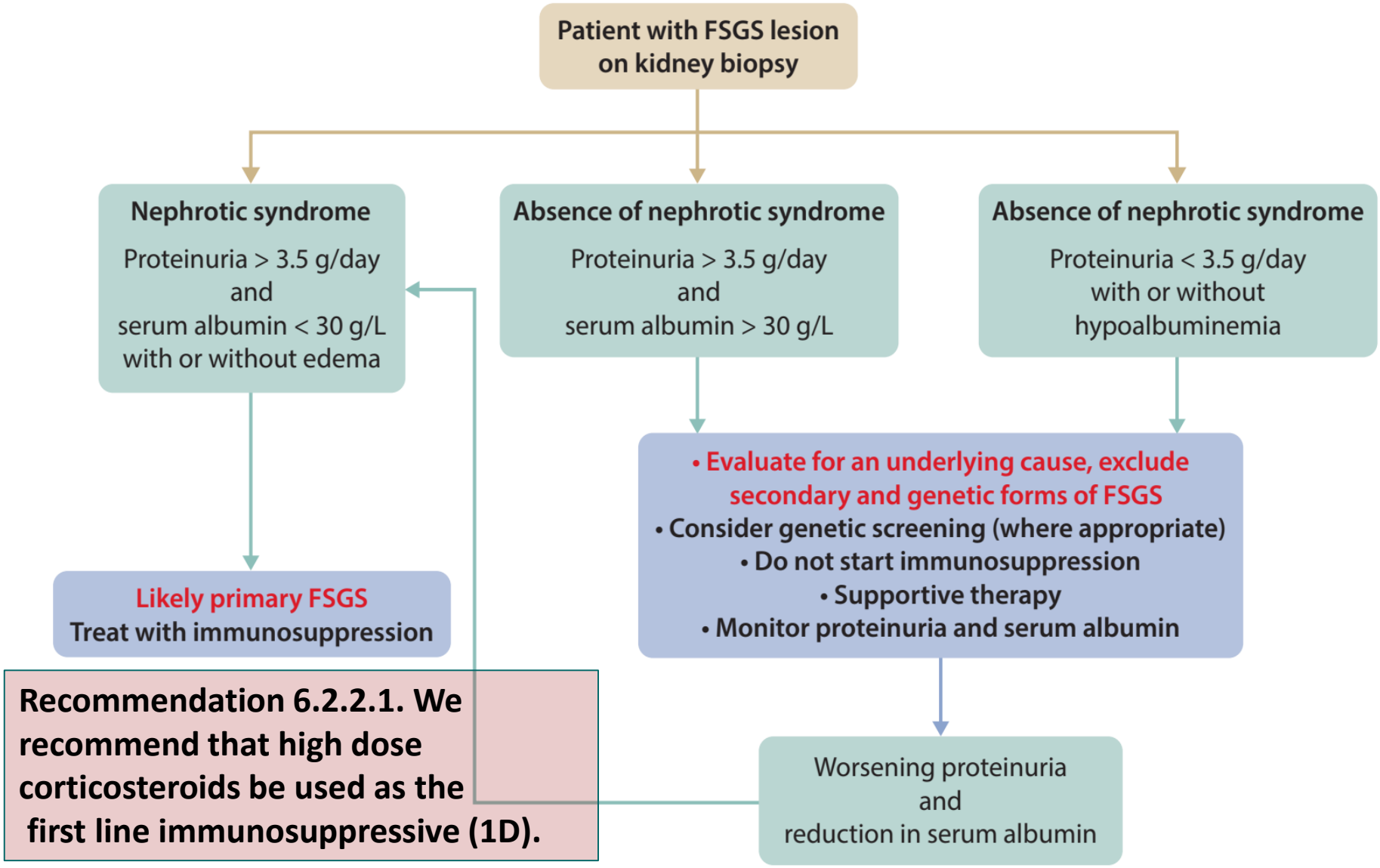
Weeks from complete remission	0	12	26	52	78
Prednisolone (number followed-up)	22 (23)	18 (23)	13 (23)	7 (21)	4 (21)
Tacrolimus (number followed-up)	22 (22)	19 (22)	15 (22)	9 (22)	6 (22)

STEROID-RESISTANT NEPHROTIC SYNDROME IN CHILDREN

Recommendation 4.4.1: We recommend using cyclosporine or tacrolimus as initial second-line therapy for children with steroid-resistant nephrotic syndrome (1C).

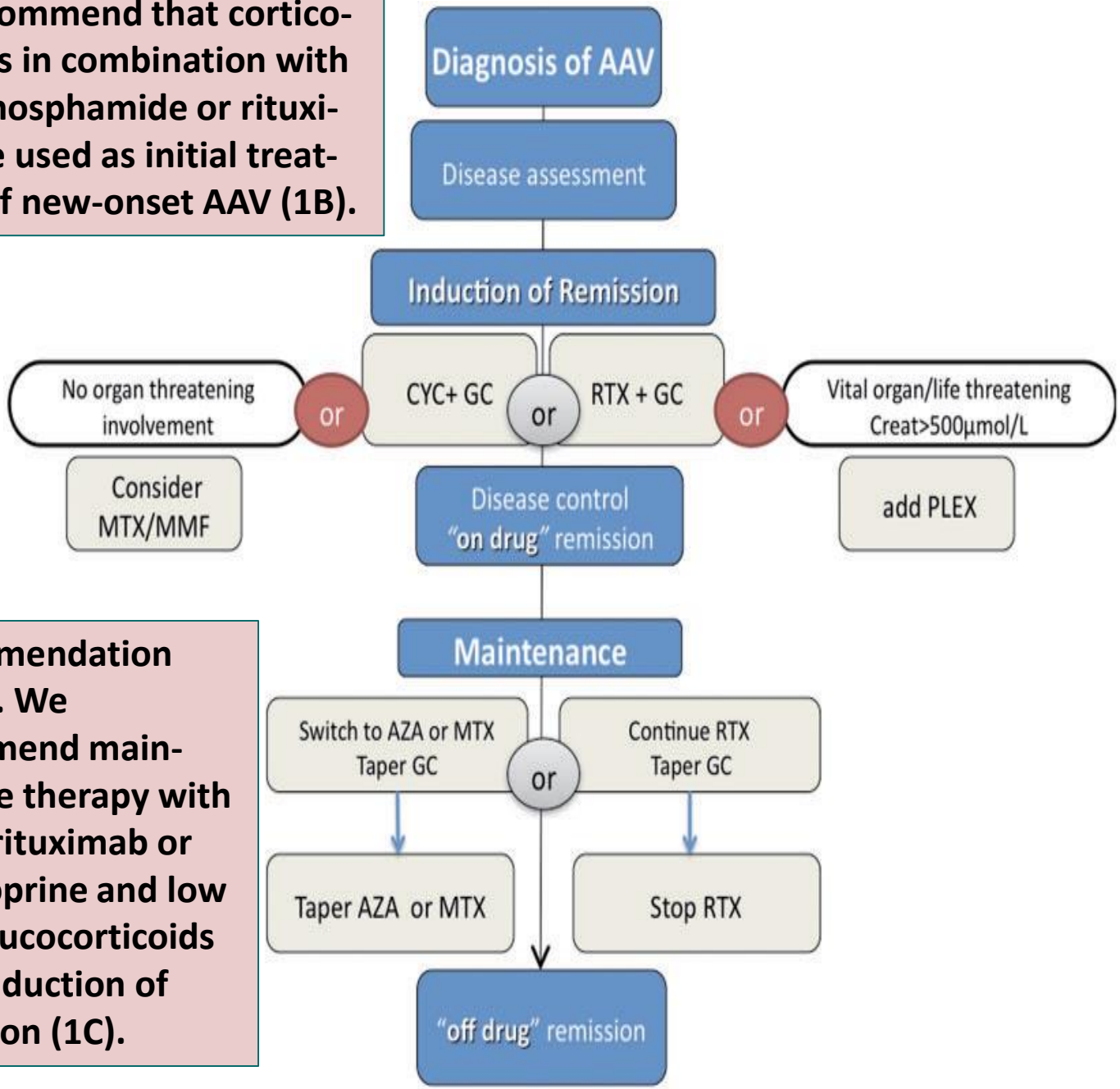
Indication for kidney biopsy*	• Children presenting with nephrotic syndrome ≥ 12 years of age • Steroid-resistant nephrotic syndrome or subsequent failure to respond to glucocorticoids in steroid-sensitive nephrotic syndrome (secondary steroid-sensitive nephrotic syndrome) • A high index of suspicion for a different underlying pathology (macroscopic hematuria, systemic symptoms of vasculitis, hypocomplementemia, etc.) • At onset, kidney failure not related to hypovolemia. Subsequently, decreasing kidney function in children receiving calcineurin inhibitors or prolonged exposure to calcineurin inhibitors (2 to 3 years)
Genetic testing	• Steroid-resistant nephrotic syndrome • Congenital and infantile forms of nephrotic syndrome (<1 year of age) • Nephrotic syndrome associated with syndromic features • Family history of steroid-resistant nephrotic syndrome or focal segmental glomerulosclerosis
Vitamin D/calcium	In patients with steroid-sensitive nephrotic syndrome and normal vitamin D levels, supplementation is not required. However, in frequent relapsing nephrotic syndrome or steroid-dependent nephrotic syndrome children or in the presence of a known vitamin D deficiency, a reduction in bone mineral content can be prevented by oral supplementation with oral calcium and vitamin D.[1,2]
Gastroprotection	There is insufficient evidence of benefit to recommend prophylactic use of proton-pump inhibitors in children with nephrotic syndrome in the absence of risk factors for gastrotoxicity or of gastric symptoms.

FSGS in adults



ANCA vasculitis

Recommendation 9.3.1.
We recommend that corticosteroids in combination with cyclophosphamide or rituximab be used as initial treatment of new-onset AAV (1B).

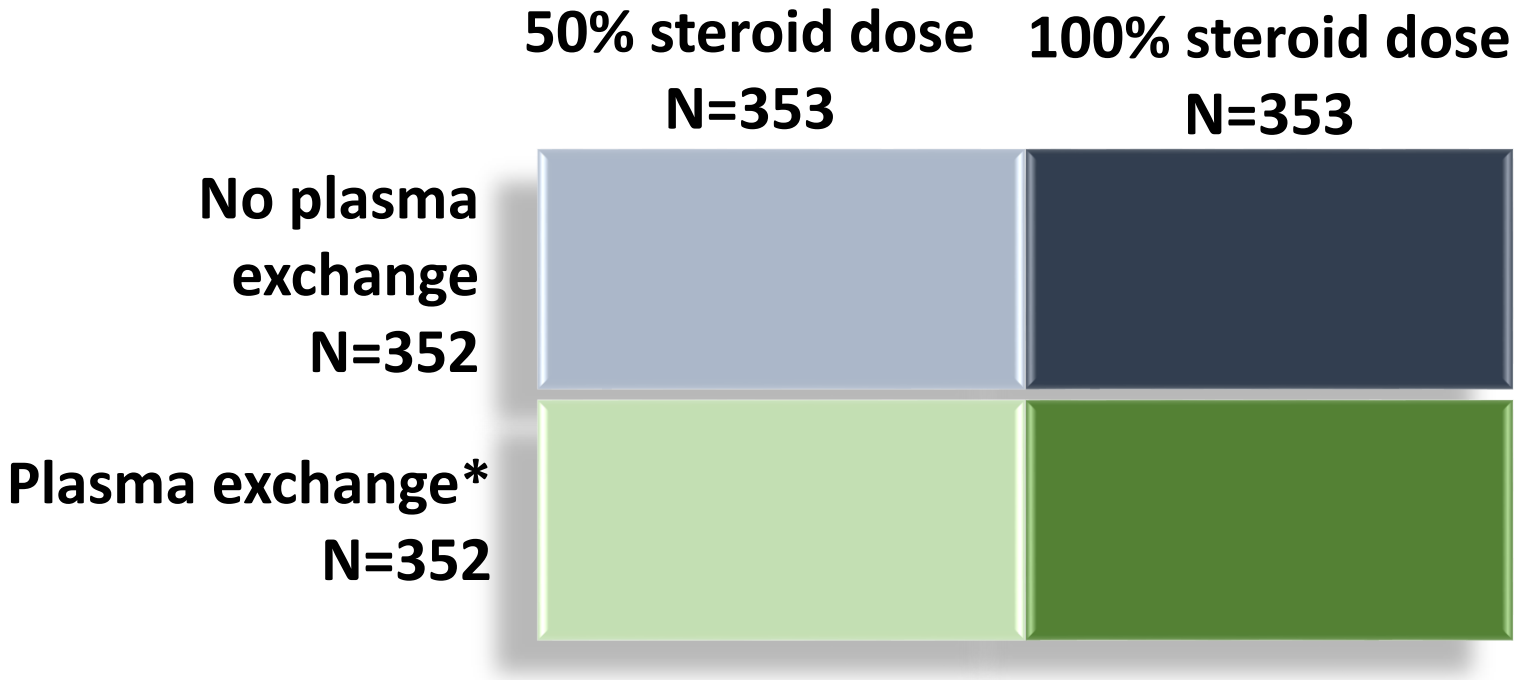


Recommendation 9.3.1.1. We recommend maintenance therapy with either rituximab or azathioprine and low dose glucocorticoids after induction of remission (1C).

Walsh M et al, N Engl J Med 2020;382:622-31

Pexivas: Plasmapheresis in severe ANCA vasculitis

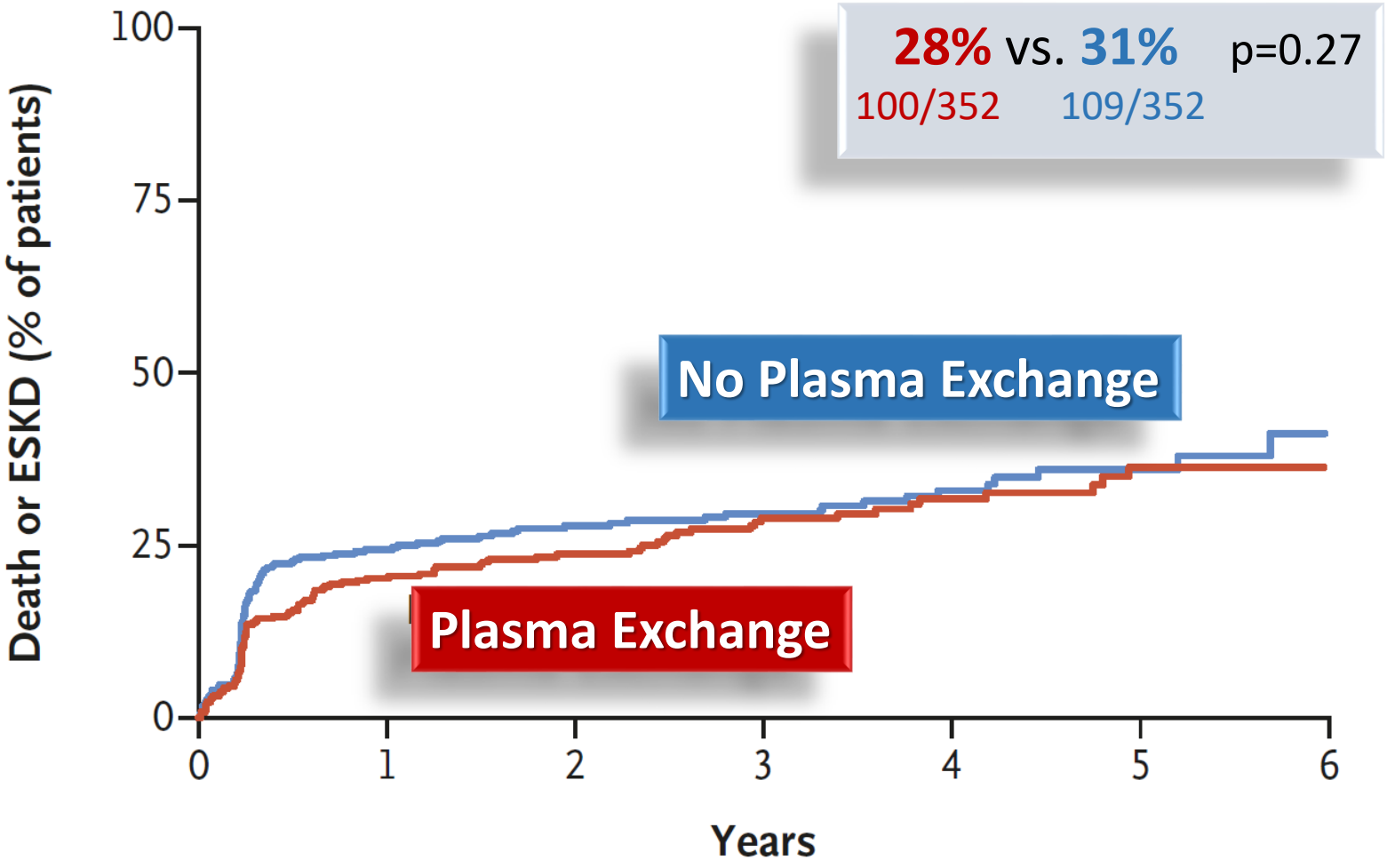
- 704 patients
- 18% pulmonary hemorrhage, 9% severe
- Median s-creatinine 327 µmol/l, 20% dialysis dependent



* 60 ml albumin/kg body weight
7x during 14 days after randomization

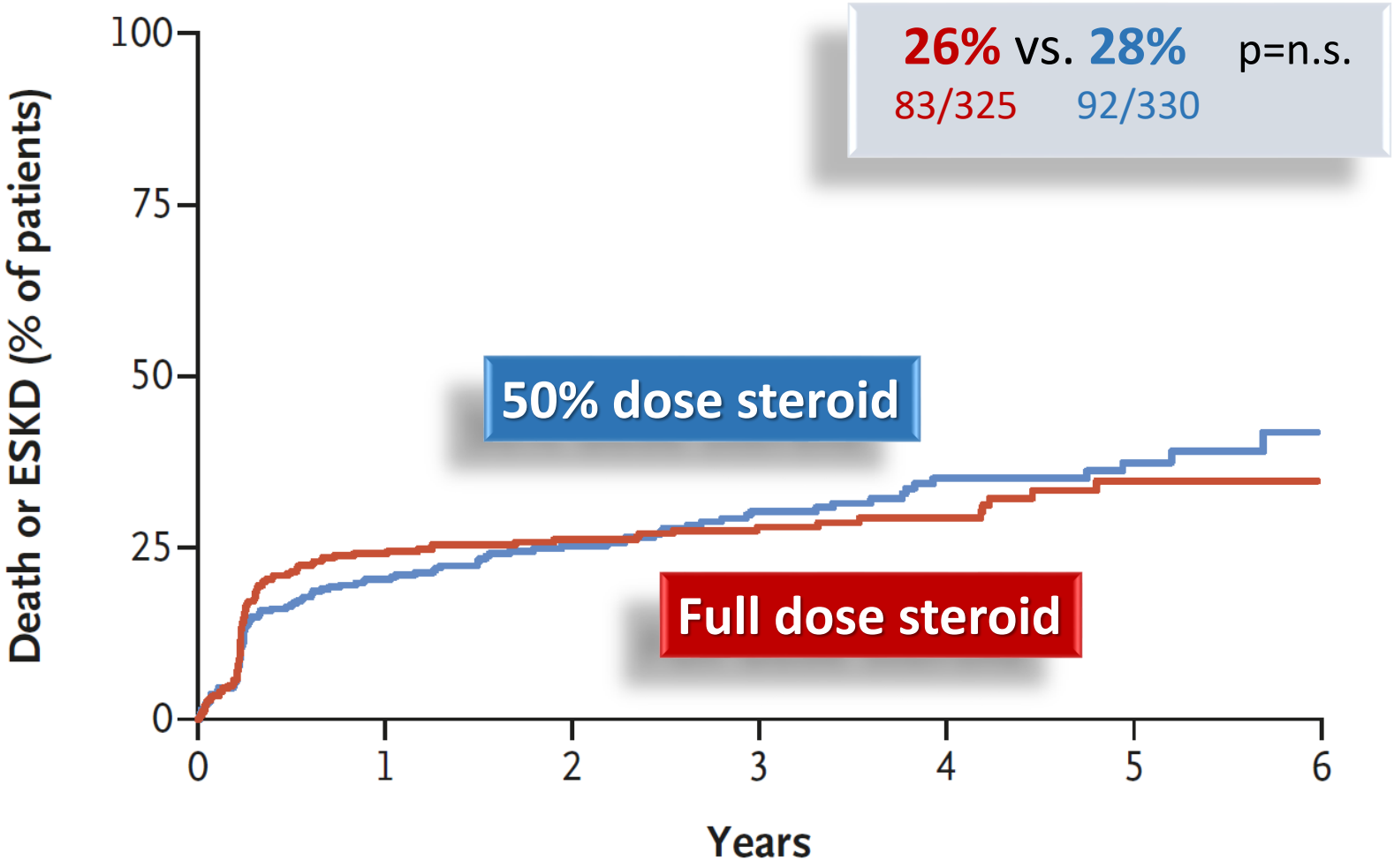
Walsh M et al, N Engl J Med 2020;382:622-31

Pexivas: Plasmapheresis in severe ANCA vasculitis



Walsh M et al, N Engl J Med 2020;382:622-31

Pexivas: Plasmapheresis in severe ANCA vasculitis



Walsh M et al, N Engl J Med 2020;382:622-31

Pexivas: Plasmapheresis in severe ANCA vasculitis

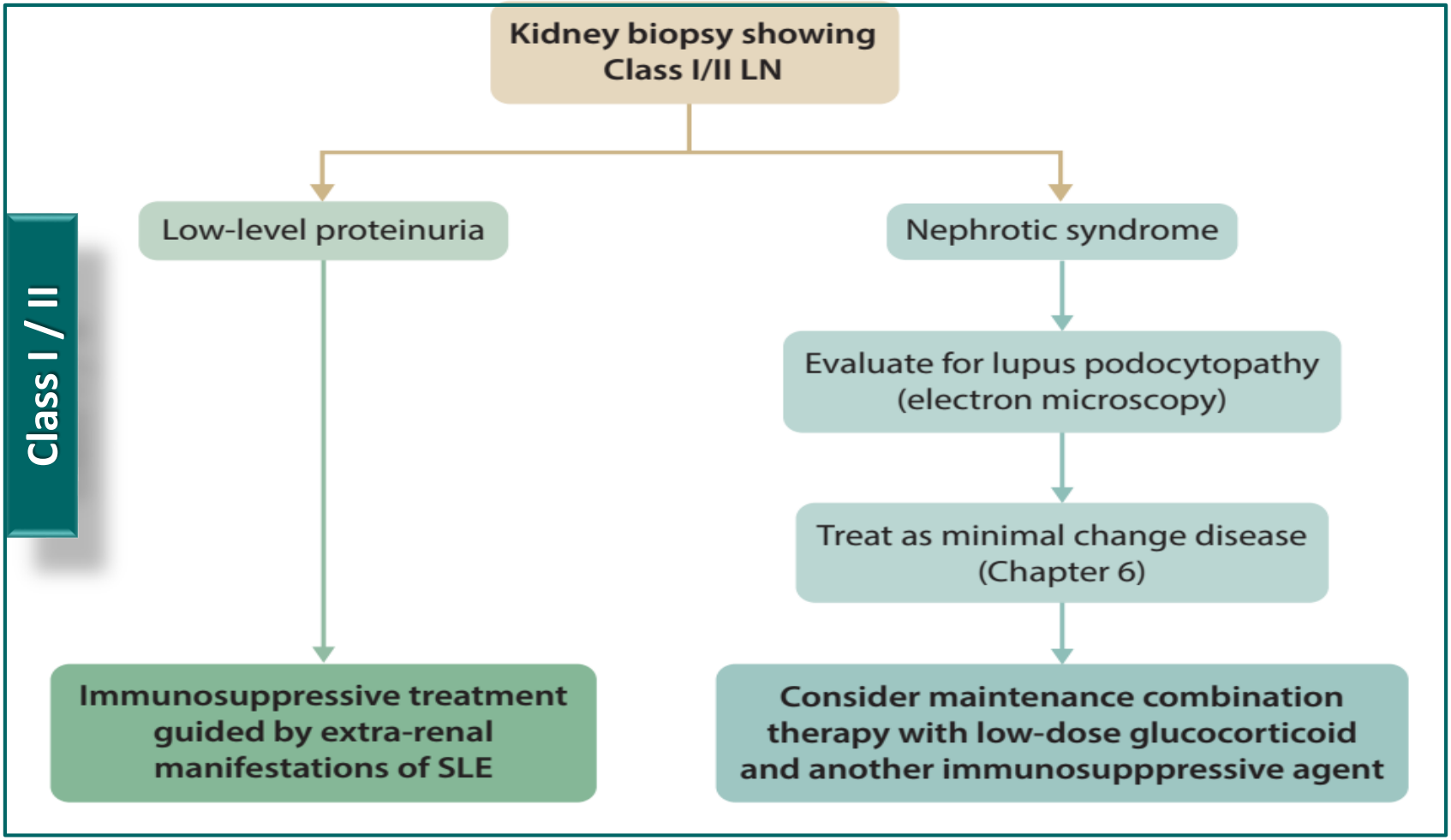
Secondary Outcome	Plasma Exchange vs. No Plasma Exchange	Reduced-Dose vs. Standard-Dose Glucocorticoid Regimen
	effect size (95% CI)	
Death from any cause	0.87 (0.58–1.29)	0.78 (0.53–1.17)
End-stage kidney disease	0.81 (0.57–1.13)	0.96 (0.68–1.34)
Sustained remission	1.01 (0.89–1.15)	1.04 (0.92–1.19)
Serious adverse events	1.21 (0.96–1.52)	0.95 (0.75–1.20)
Serious infections at 1 year	1.16 (0.87–1.56)	0.69 (0.52–0.93)

ANCA vasculitis

Week	"Reduced-corticosteroid dose" in PEXIVAS trial		
	<50 kg	50-75 kg	>75 kg
1	50	60	75
2	25	30	40
3-4	20	25	30
5-6	15	20	25
7-8	12.5	15	20
9-10	10	12.5	15
11-12	7.5	10	12.5
13-14	6	7.5	10
15-16	5	5	7.5
17-18	5	5	7.5
19-20	5	5	5
21-22	5	5	5
23-52	5	5	5
>52	Investigators' Local Practice		

Lupus nephritis

Recommendation 10.2.1.1. We recommend that patients with LN be treated with hydroxychloroquine or an equivalent antimalarial unless contraindicated (1C).



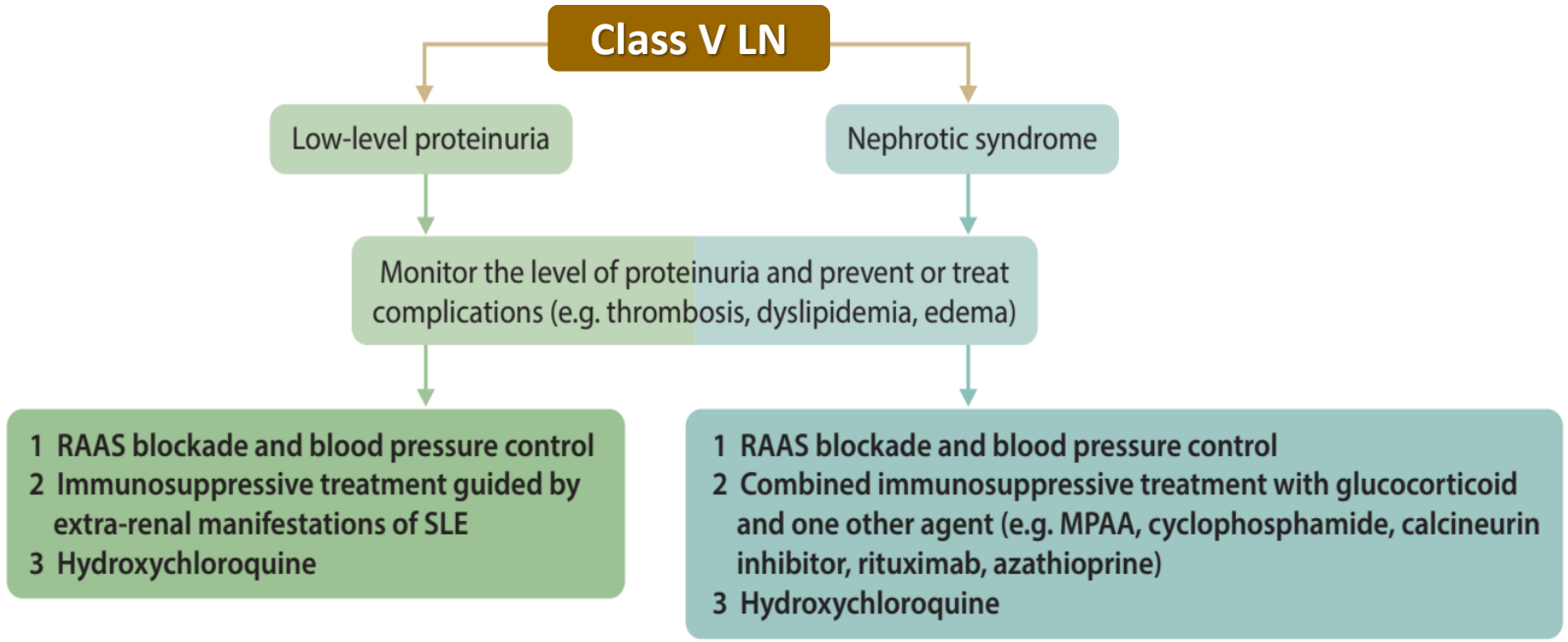
Lupus nephritis

Class III or IV

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 corticosteroids plus either low dose i.v. cyclophosphamide or MPAA (1B).

Recommendation 10.2.3.2.1. We recommend that after completion of initial therapy patients should be placed on MPAA for maintenance (1B).

Class V



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