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Management and treatment of glomerular diseases: Highlights of the 2020 KDIGO guideline

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UNIKLINIK RWTH AACHEN

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: 2020 KDIGO clinical practice guideline on glomerular diseases

Draft version! Public review June 2020

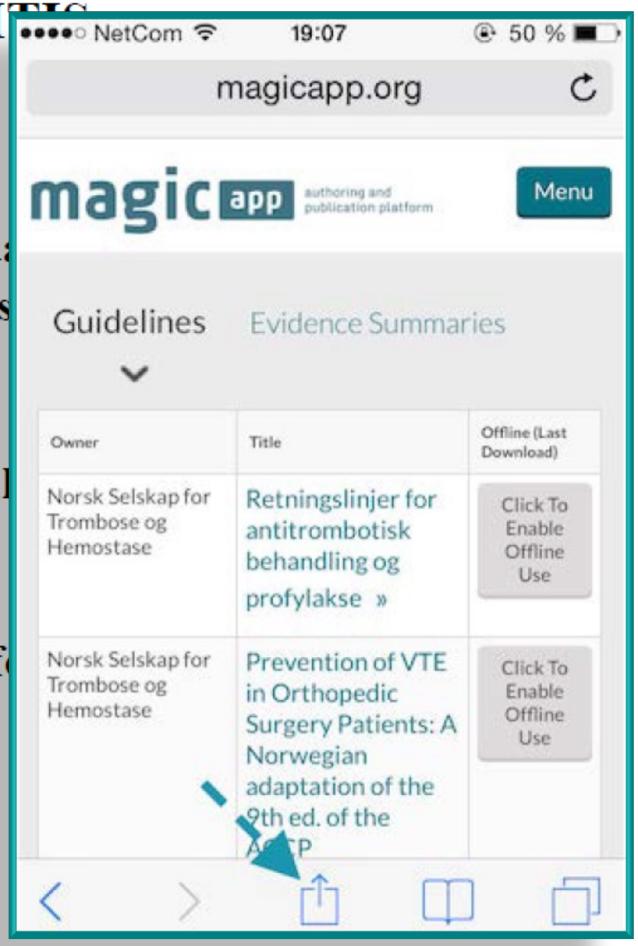
CHAPTER 1. GENERAL PRINCIPLES FOR THE MANAGEMENT OF GLOMERULONEPHRITIS

1.1. Kidney biopsy

Practice Point 1.1.1. The kidney biopsy is the "gold standa
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.



2020 KDIGO clinical practice guideline on glomerular diseases

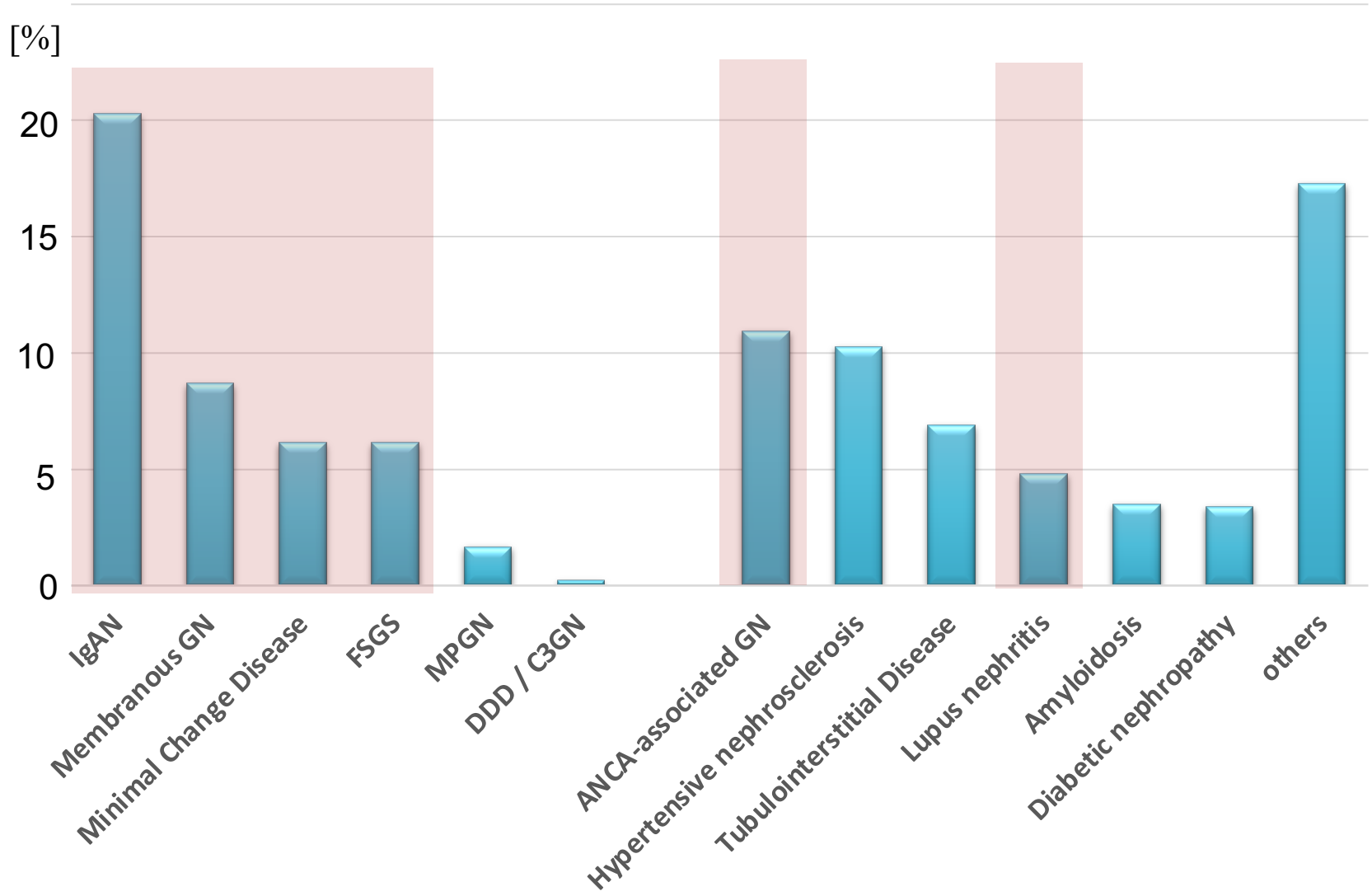
Draft version!
Public review June 2020

CHAPTER 1. GENERAL PRINCIPLES FOR THE MANAGEMENT OF
RULONEPHRITIS

60 written pages……

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

Draft version!
Public review June 2020

2.2. Prognosis 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 *prognostic* 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

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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

Draft version!
Public review June 2020

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).

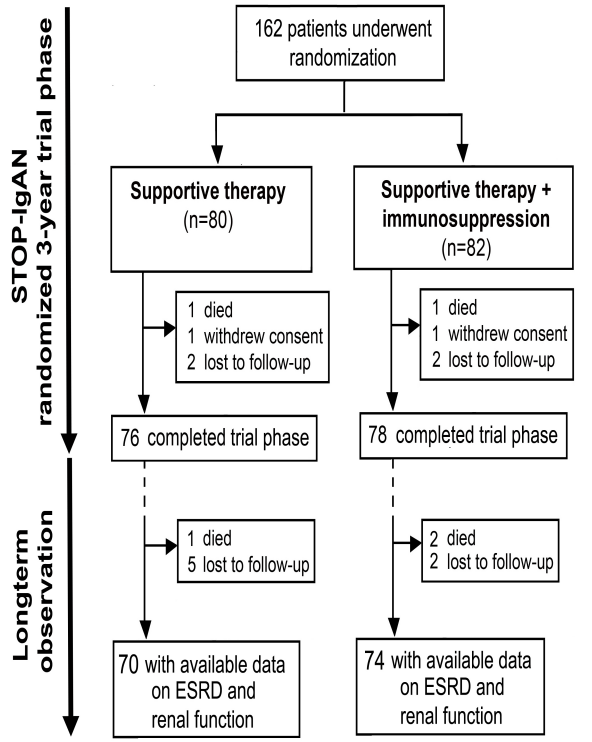
Use extreme caution or avoided entirely if:
eGFR < 30 mL/min/1.73 m^2 *
Diabetes
Obesity (BMI > 30 kg/m^2) **
Latent infections (e.g. hepatitis, TB)
Secondary disease (e.g. cirrhosis)
Active peptic ulceration
Uncontrolled psychiatric illness

Rauen T, …. Floege J. Kidney Int 2020 in press

STOP-IgAN trial: Long-term Renal Outcomes

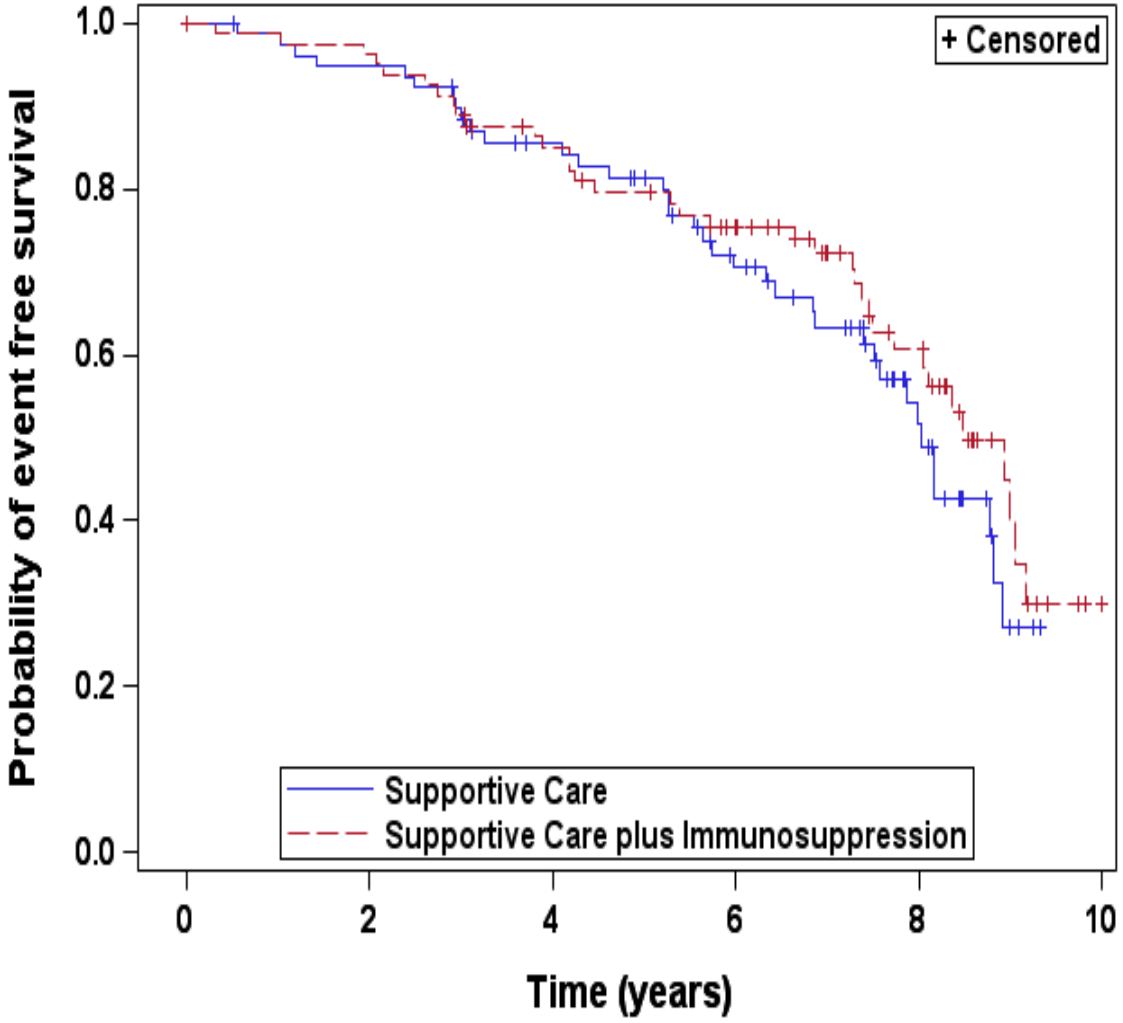
Long-term

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

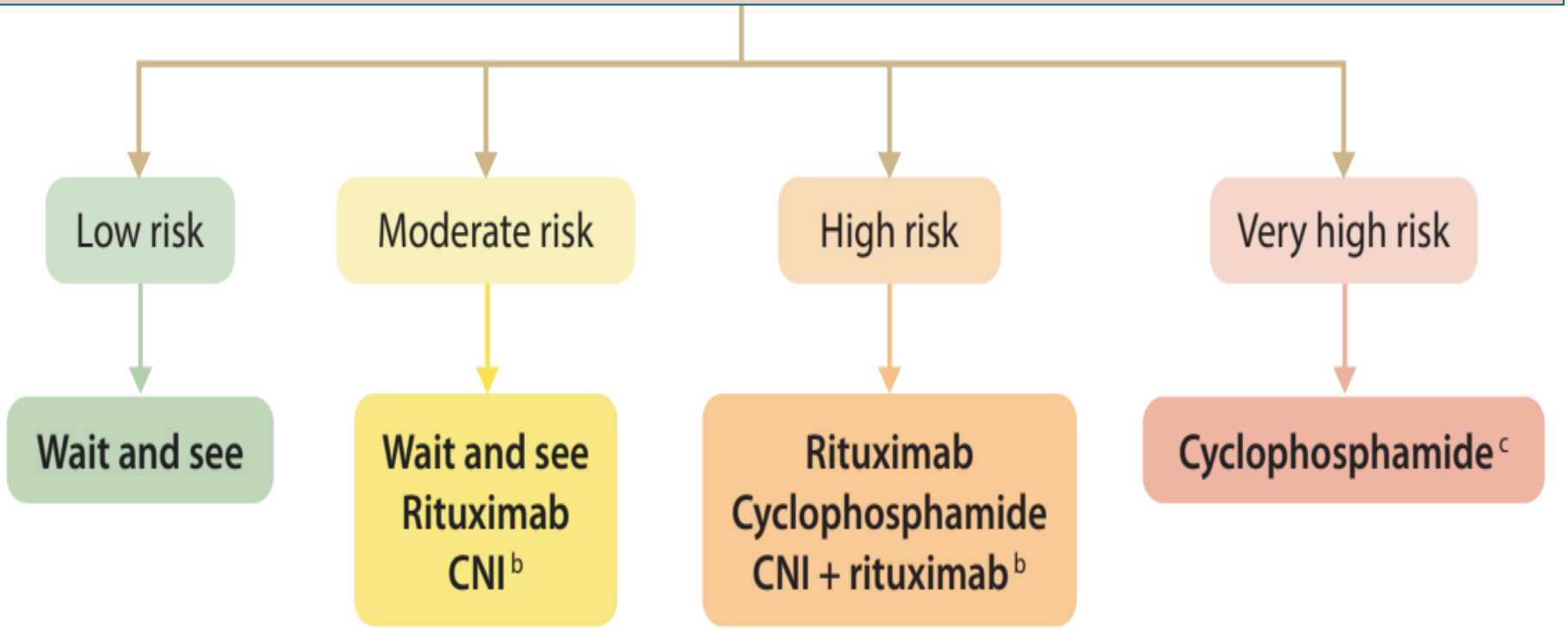
Draft version! Public review June 2020

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 in membranous GN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rituximab or Cyclosporine in the Treatment of Membranous Nephropathy

1 g on d1+d14

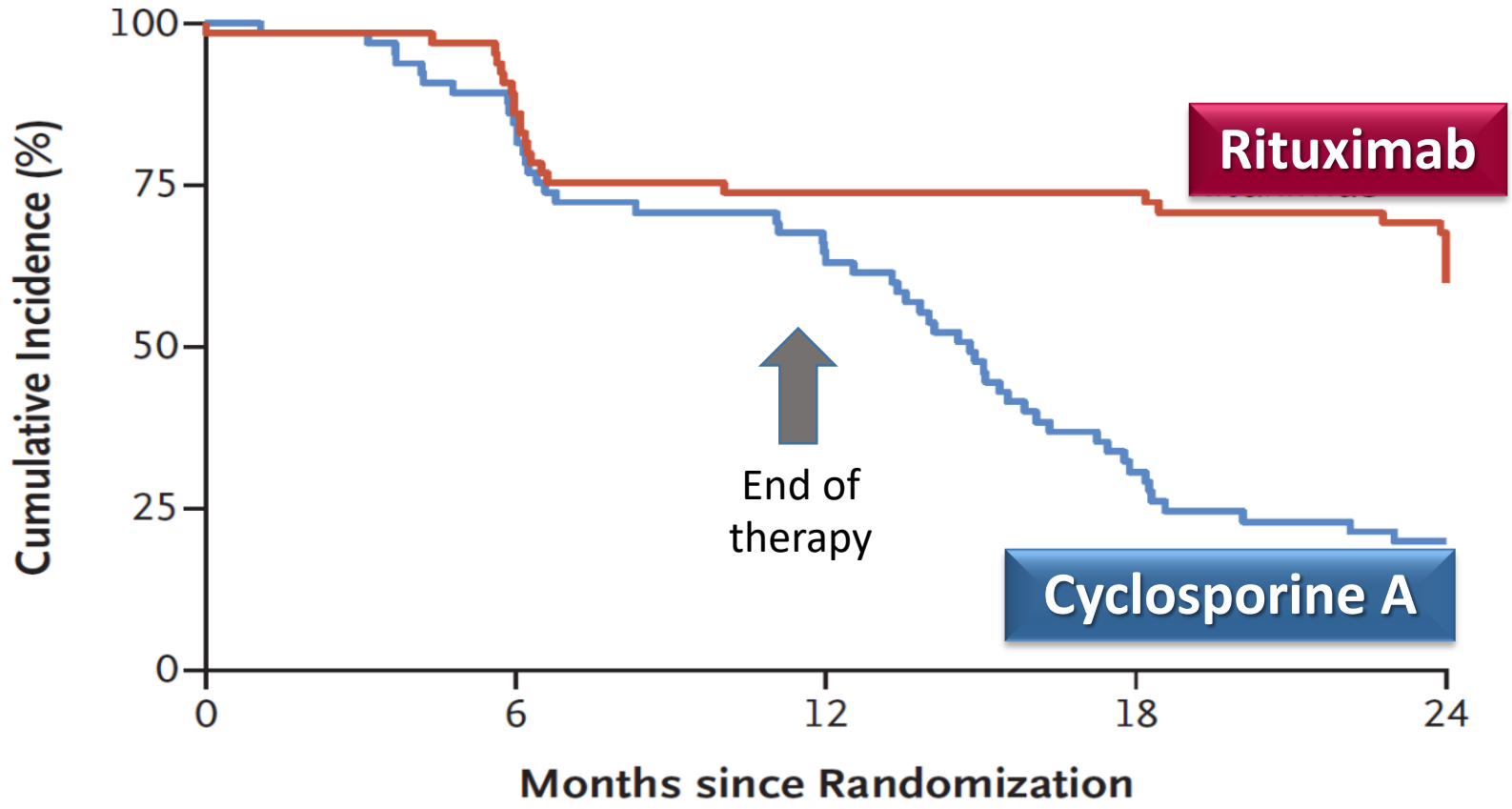
F.C. Fervenza, G.B. Appel, S.J. Barbour, B.H. Rovin, R.A. Lafayette, N. Aslam, J.A. Jefferson, P.E. Gipson, D.V. Rizk, J.R. Sedor, J.F. Simon, E.T. McCarthy, P. Brenchley, S. Sethi, C. Avila-Casado, H. Beanlands, J.C. Lieske, D. Philibert, T. Li, L.F. Thomas, D.F. Green, L.A. Juncos, L. Beara-Lasic, 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

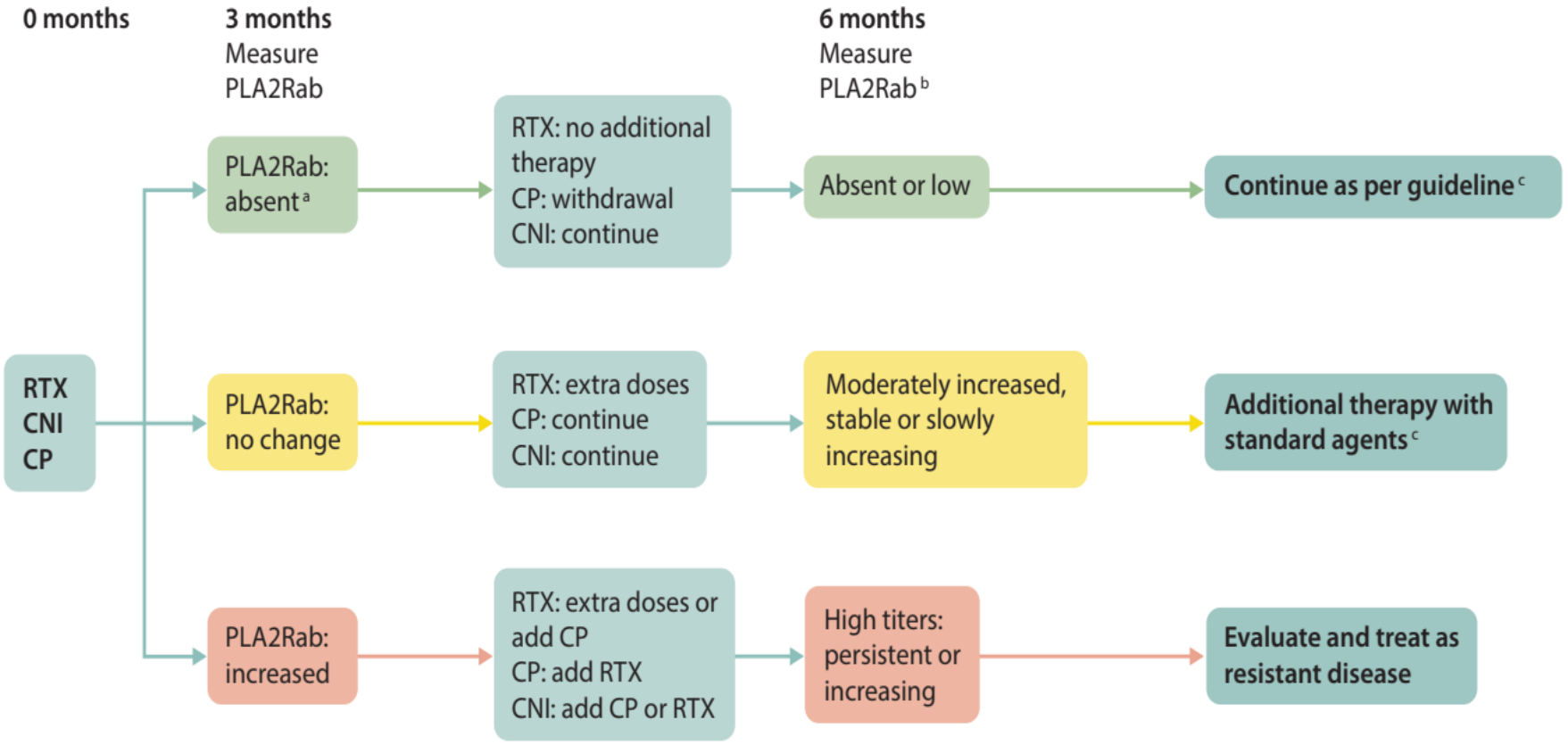


No. at Risk					
Rituximab	65	59	48	48	44
Cyclosporine	65	56	42	20	13

Membranous nephropathy

Draft version!
Public review June 2020

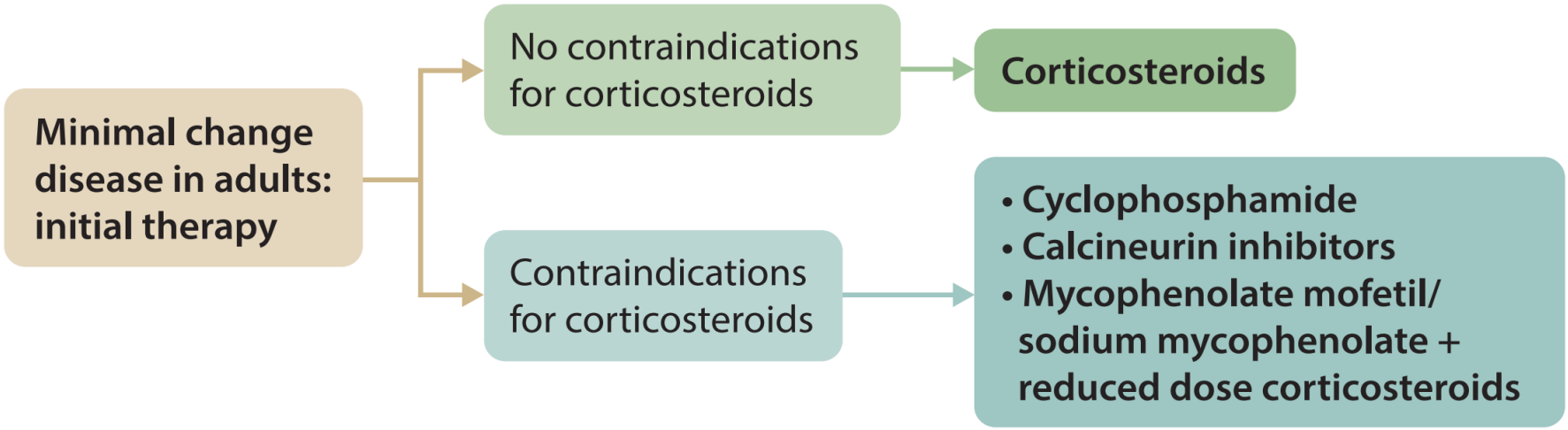
Practice Point 3.3.3. Longitudinal monitoring of PLA2Rab levels at three and six months after start of therapy may be useful for evaluating treatment response in patients with membranous nephropathy, and can be used to guide adjustments to therapy



Minimal Change Disease in adults

Draft version!
Public review June 2020

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).

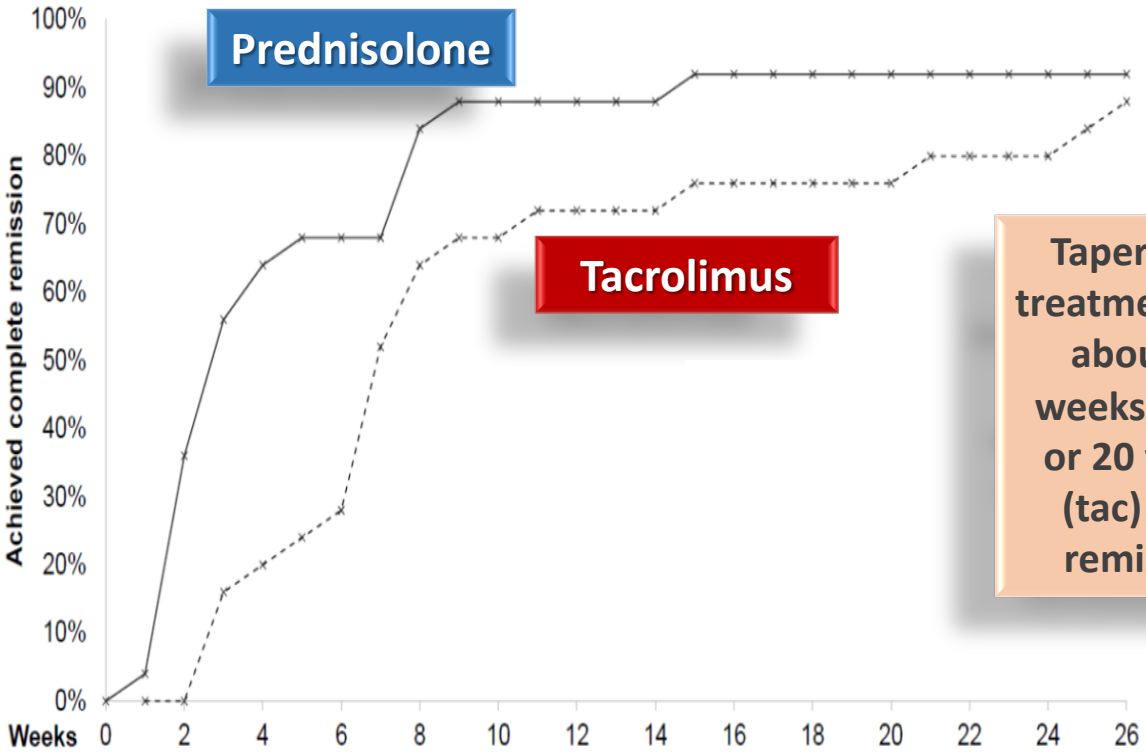
Minimal Change

Tacrolimus versus corticosteroid monotherapy for adult minimal change nephropathy

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

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

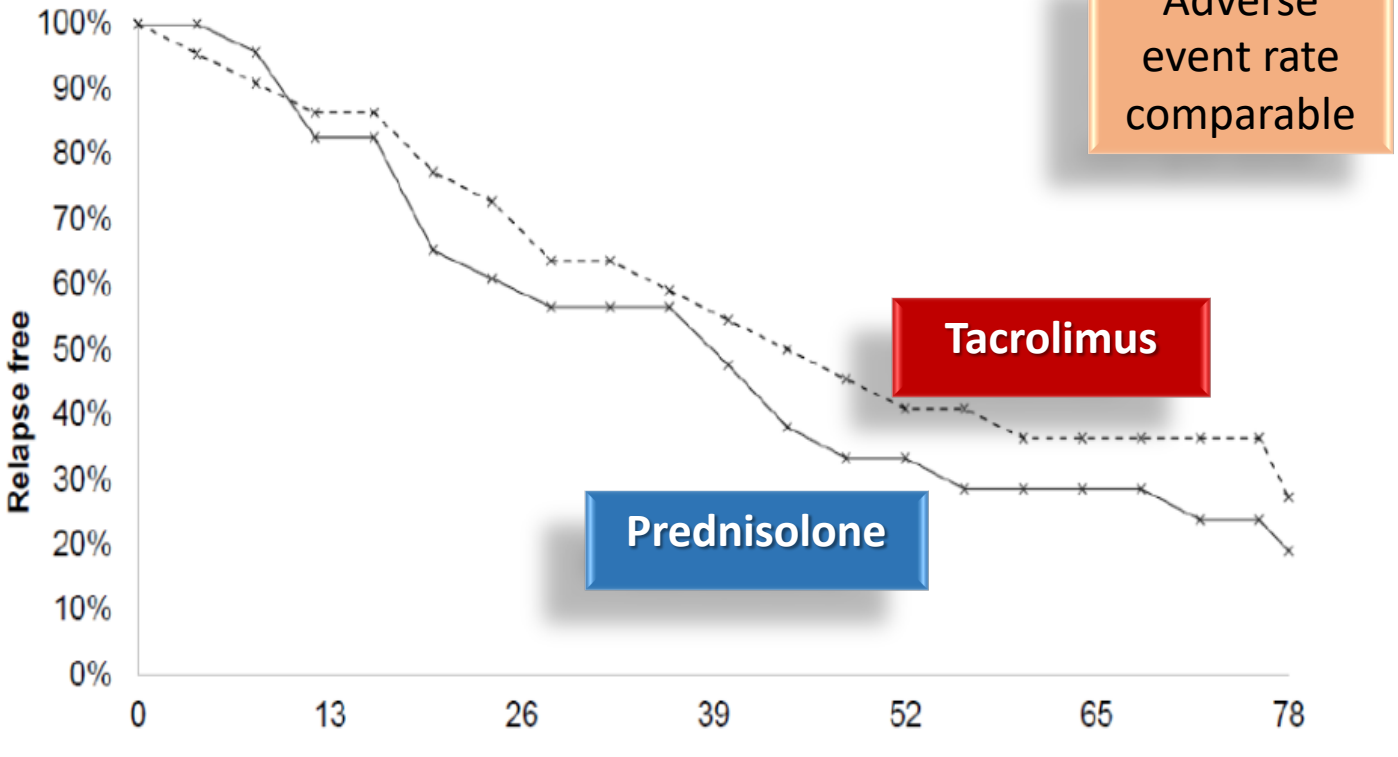
Medjeral-Thomas NR et al, CJASN 15: 209–218, 2020

Minimal Change

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)

FSGS in adults

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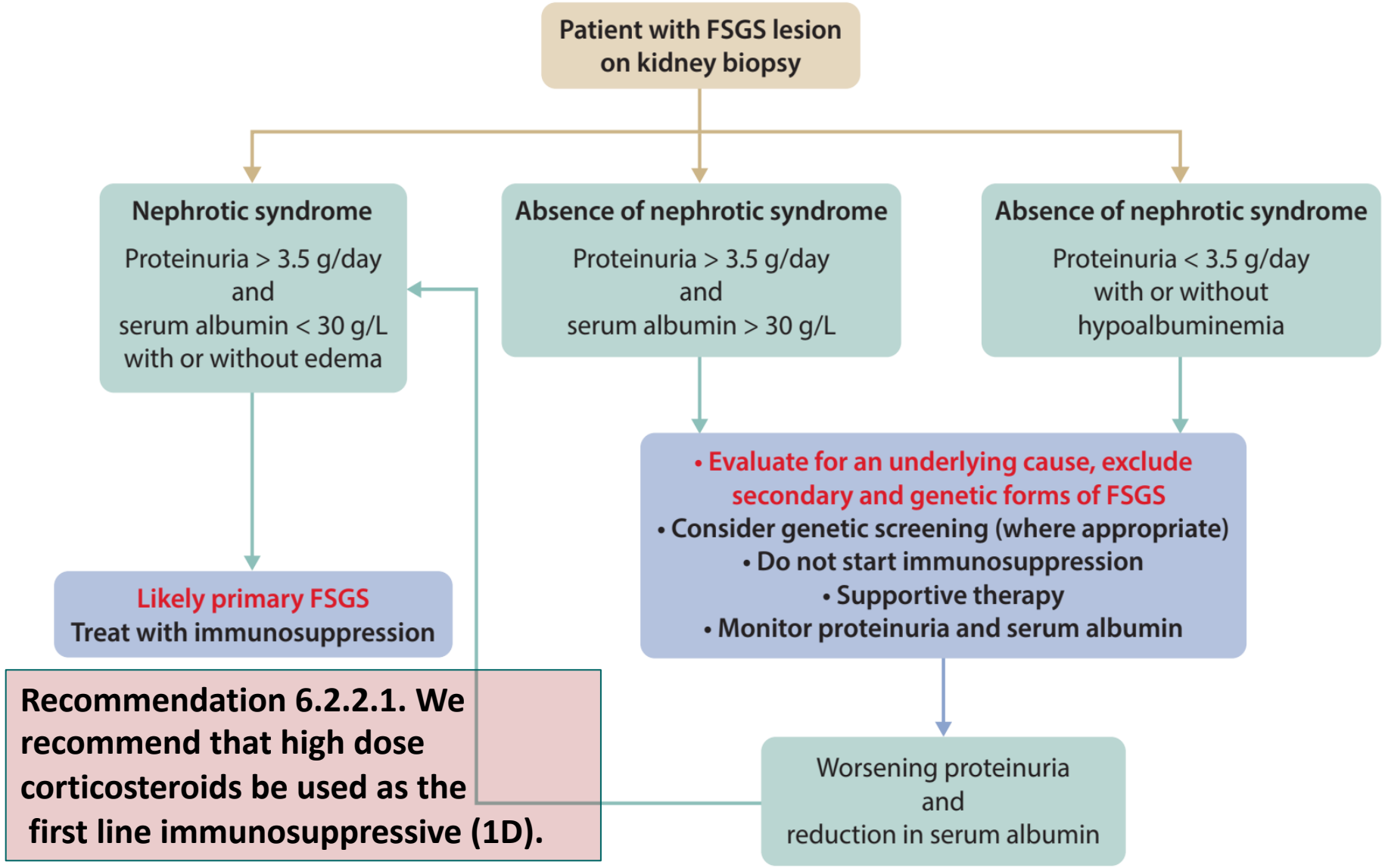

Recommendation 6.2.2.1. We recommend that high dose corticosteroids be used as the first line immunosuppressive (1D).

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).

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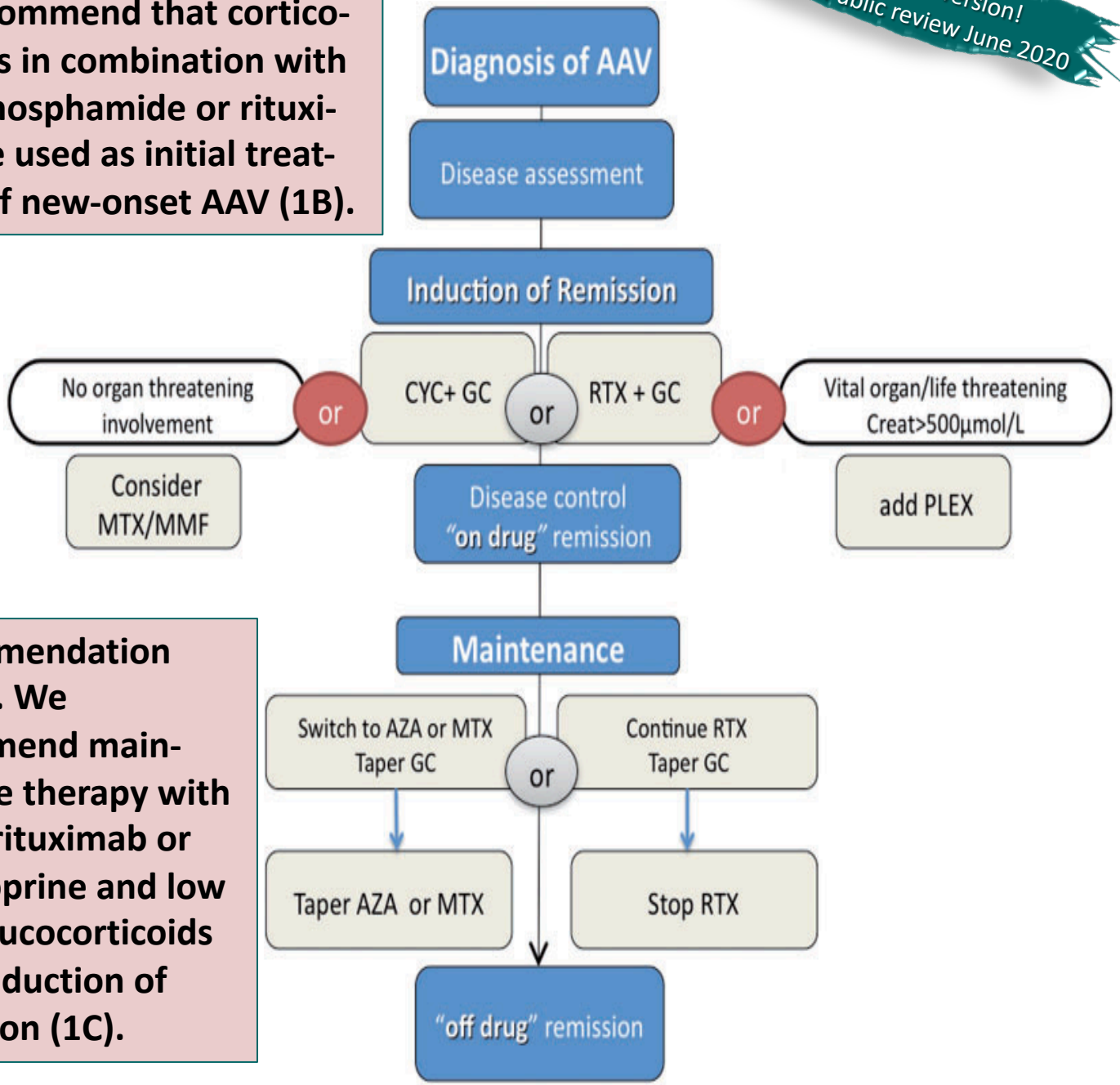
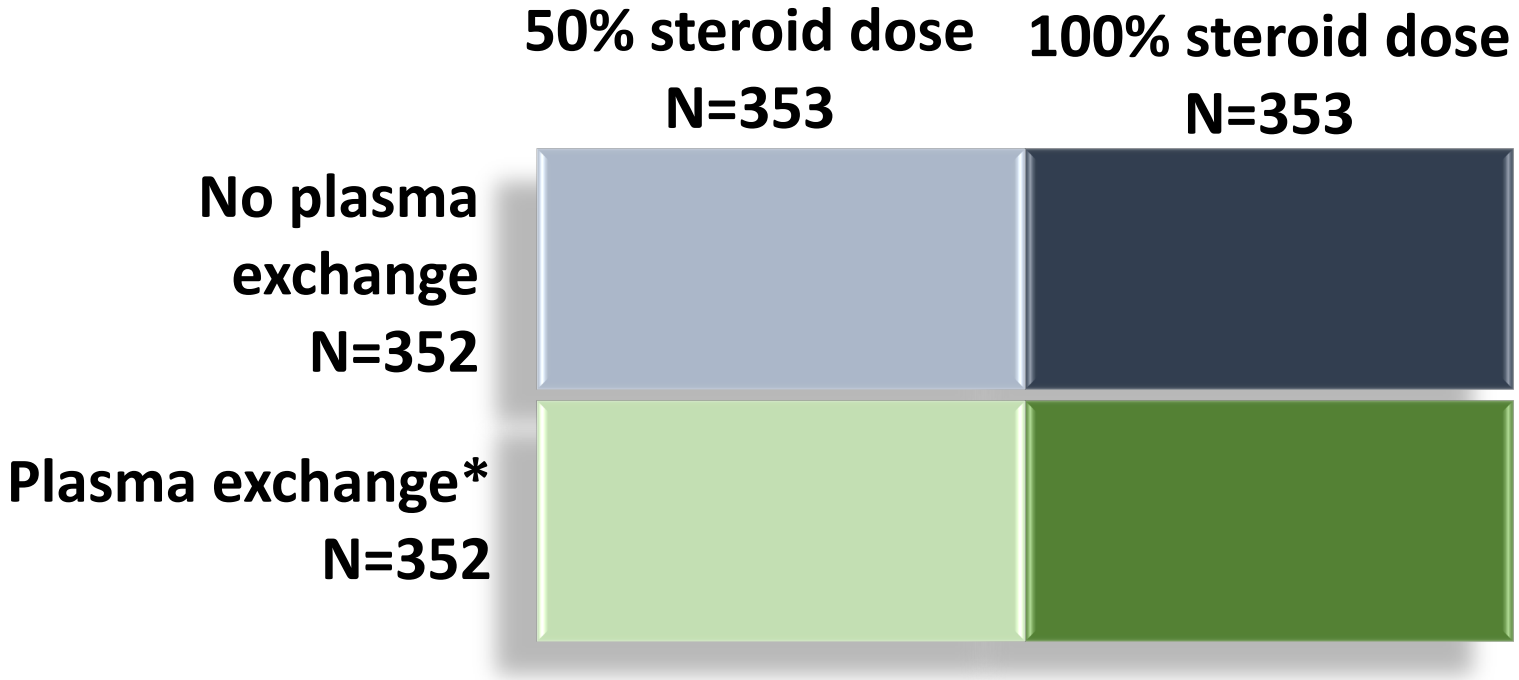


Recommendation 9.3.1.1. We recommend maintenance therapy with either rituximab or azathioprine and low dose glucocorticoids after induction of remission (1C).

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

Pexivas: Plasmapheresis in severe ANCA vasculitis

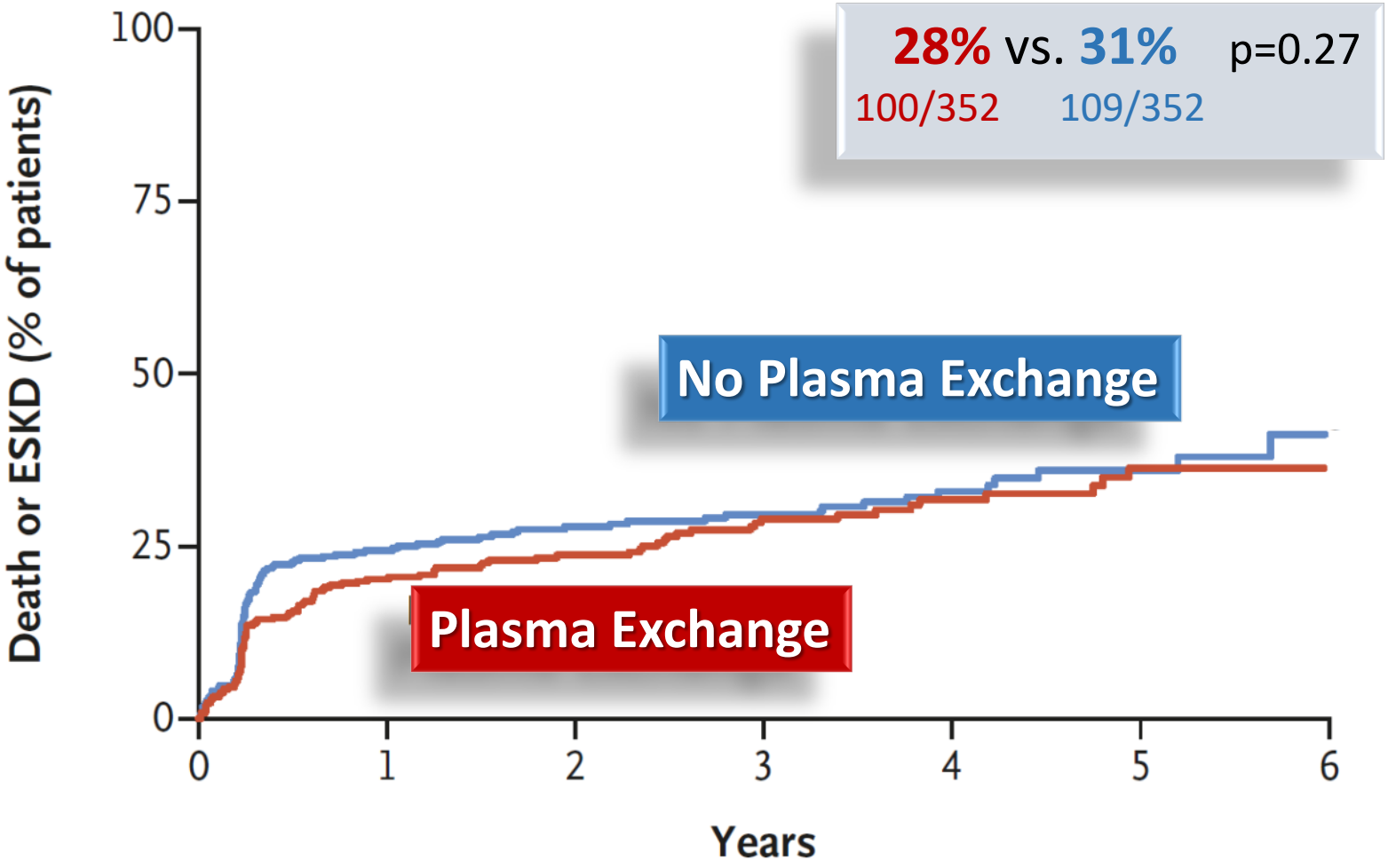
- 704 patients
- 18% pulmonary hemorrhage, 9% severe
- Median s-creatinine 327 µmol/l, 20% dialysis dependent



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

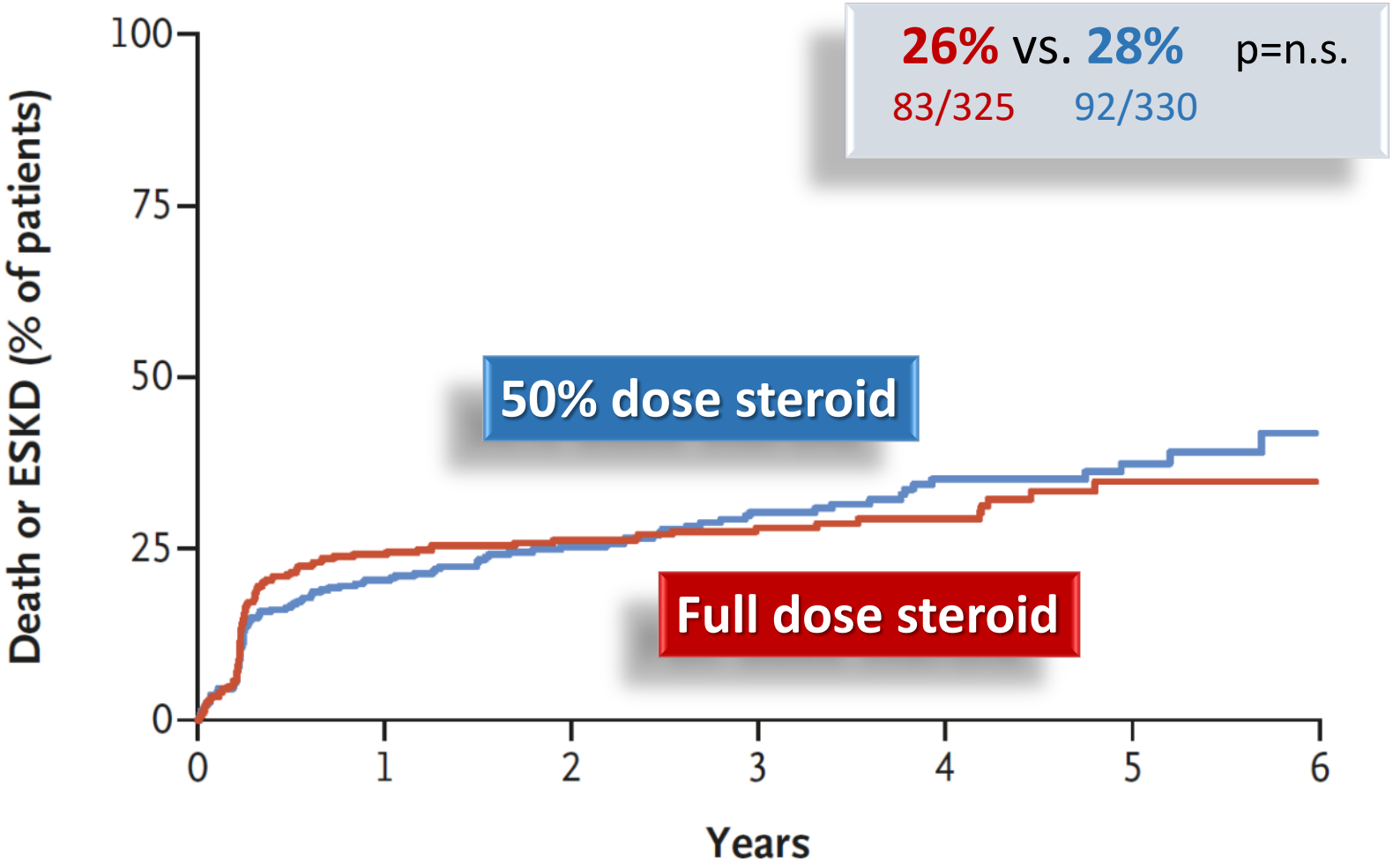
Walsh M et al, N Engl J Med 2020;382:622-31

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		

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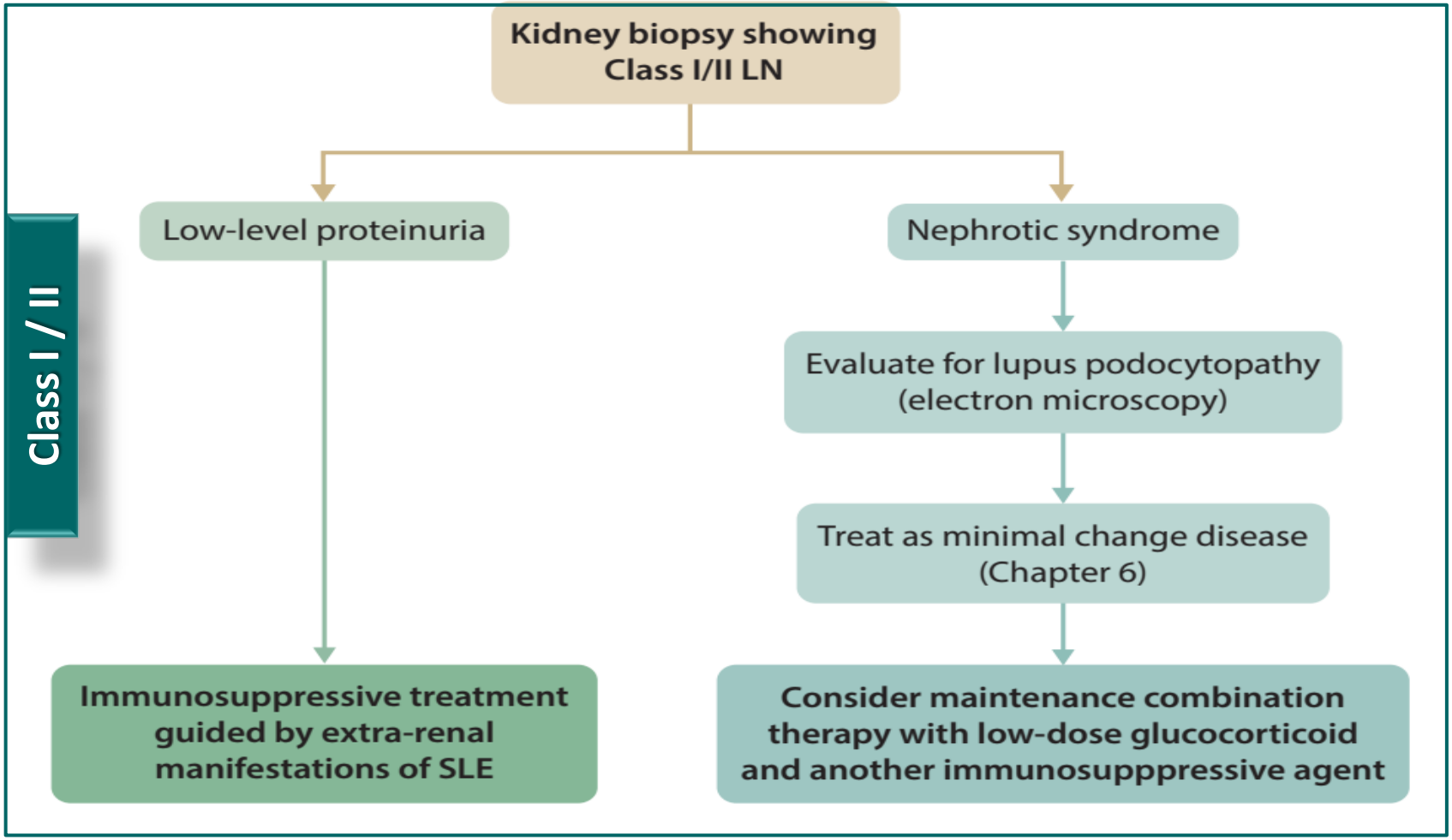
Public review June 2020

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