The 2024 updates of the KDIGO glomerular disease guidelines

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Conflicts of Interest J. Floege:

Consultancy and/or lecture honoraria: **AstraZeneca, Boehringer, CSL Vifor, GSK, Otsuka**

Data Safety Monitoring Boards: **NovoNordisk, Visterra**

Coordinator: **KDIGO guidelines on the management of glomerular diseases**

www.kidney-international.org

KDIGO executive conclusions

Kidney International (2021) **100,** 753–779

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

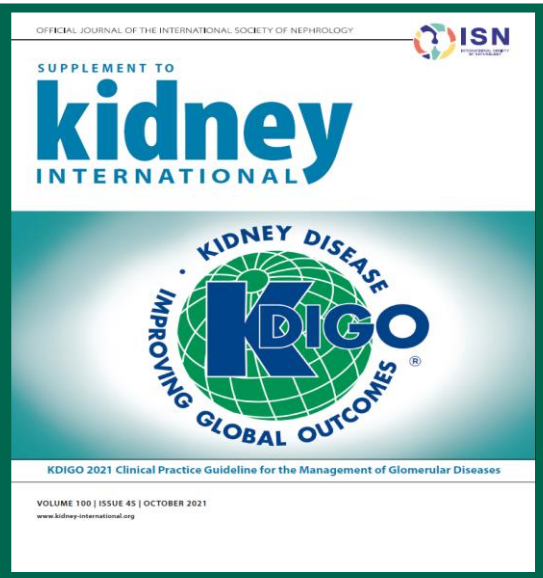
Check for updates

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 L. Gibson[9], Richard J. Glassock[10], David R.W. Jayne[11], Vivekanand Jha[12,13,14], Adrian Liew[15], Zhi-Hong Liu[16], Juan M. Mejía-Vilet[17], Carla M. Nester[18], Jai Radhakrishnan[19], Elizabeth M. Rave[20], Heather N. Reich[21], Pierre Ronco[22,23], Jan-Stephan F. Sanders[24], Sanjeev Sethi[25], Yusuke Suzuki[26], Sydney C.W. Tang[6], Vladimír Tesar[27], Marina Vivarelli[28], Jack F.M. Wetzels[29], Lyubov Lytvyn[30,31], Jonathan C. Craig[32,33], David J. Tunnicliffe[33,34], Martin Howell[33,34], Marcello A. Tonelli[35], Michael Cheung[36], Amy Earley[36] and Jürgen Floege[37]

26 pages

….or, if you like a little more detail (281 pages):



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KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases

Lupus Nephritis

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KDIGO executive conclusions

Executive summary of the KDIGO 2024 Clinical Practice Guideline for the Management of Lupus Nephritis

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OPEN

Brad H. Rovin[1], Isabelle M. Ayoub[1], Tak Mao Chan[2], Zhi-Hong Liu[3], Juan M. Mejía-Vilet[4], Ethan M. Balk[5], Craig E. Gordon[6], Gaelen Adam[5], Marcello A. Tonelli[7], Michael Cheung[8], Amy Earley[8] and Jürgen Floege[9]

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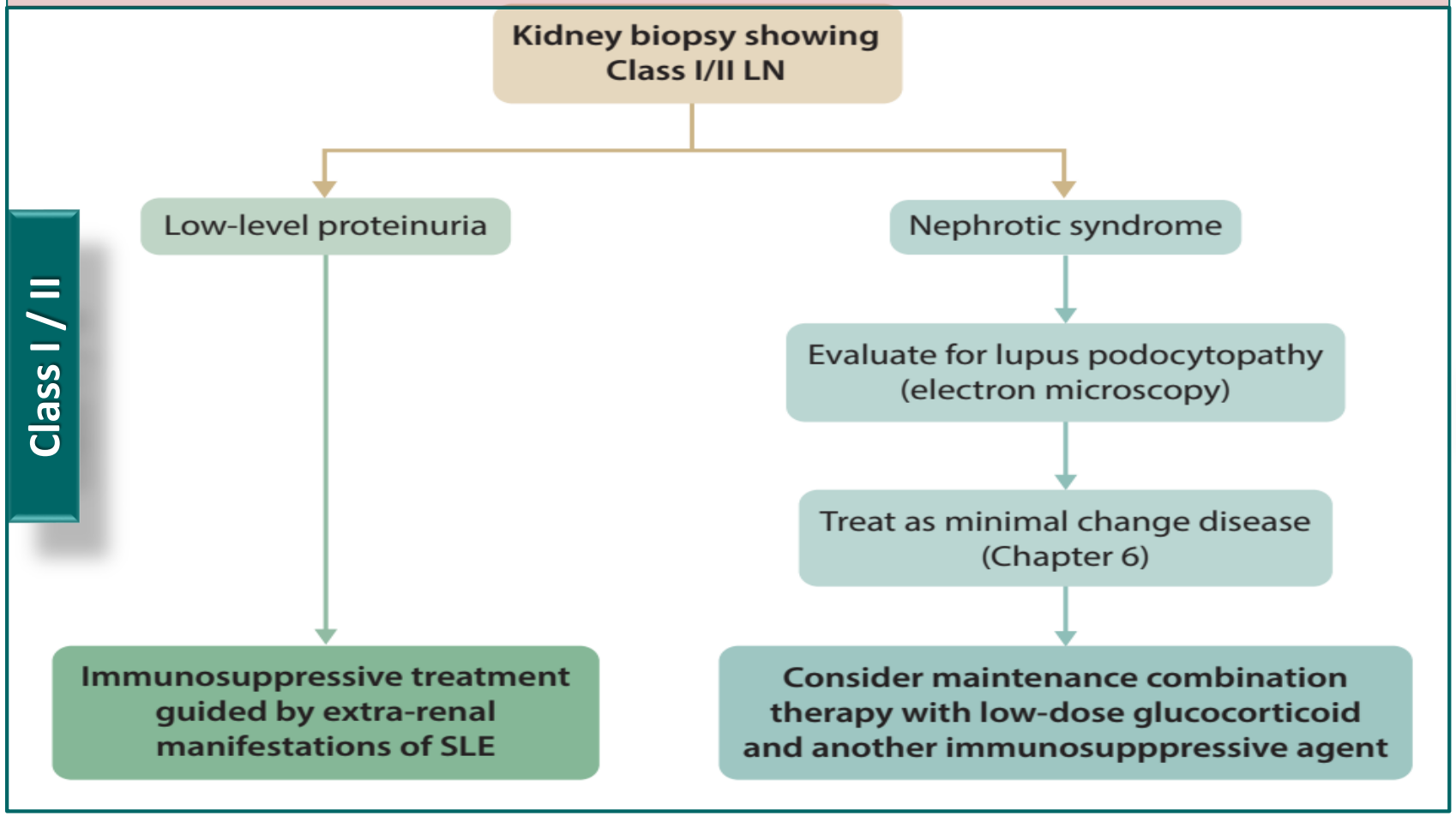
Kidney International (2024) **105,** 31–34

KDIGO 2021 Guideline and 2024 update: Lupus nephritis

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

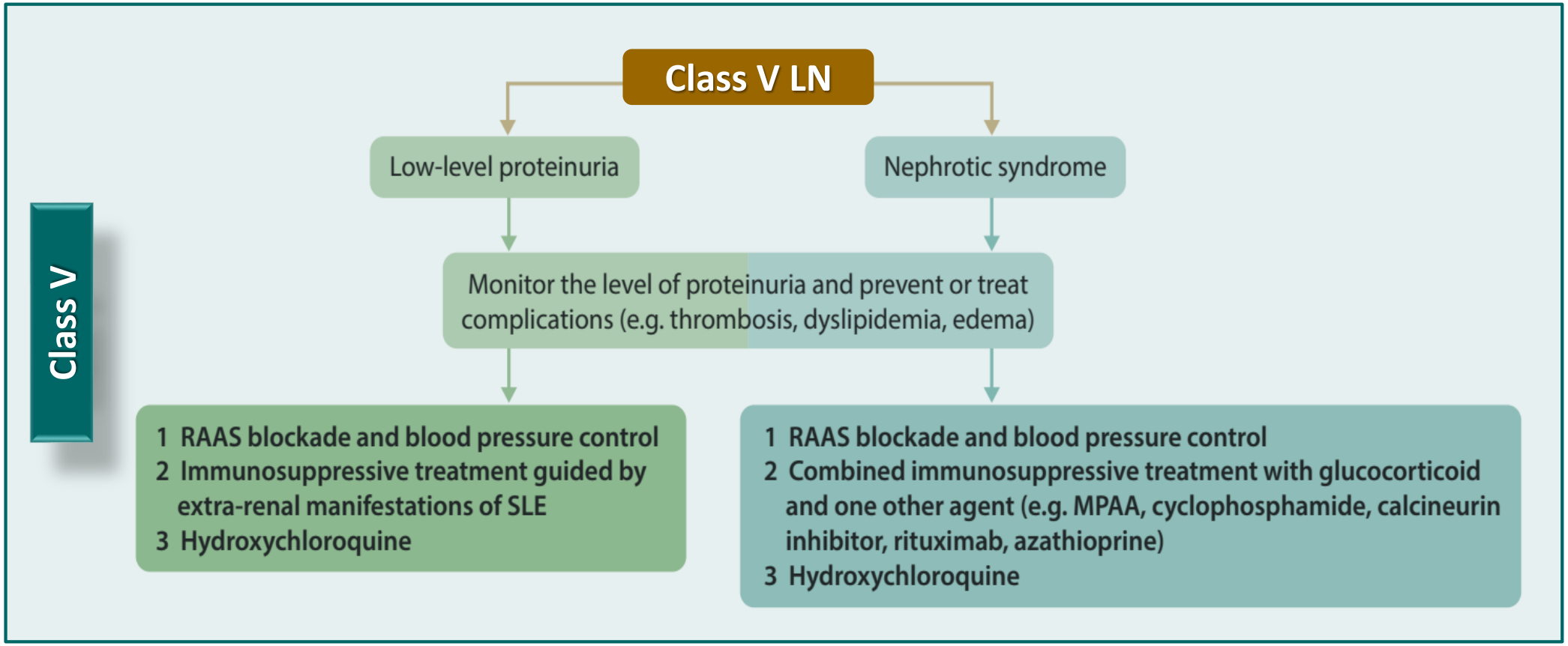
2024 update*: no change



2024 update*: no change

* KDIGO. Kidney Int 2021;100:S1–S276 and Kidney Int 2024; 105: 31-34

KDIGO 2021 Guideline and 2024 update: Lupus nephritis



2024 update*: no change

* KDIGO. Kidney Int 2021;100:S1–S276 and Kidney Int 2024; 105: 31-34

KDIGO. Kidney Int 2021;100:S1–S276 and Kidney Int 2024; 105: 31-34

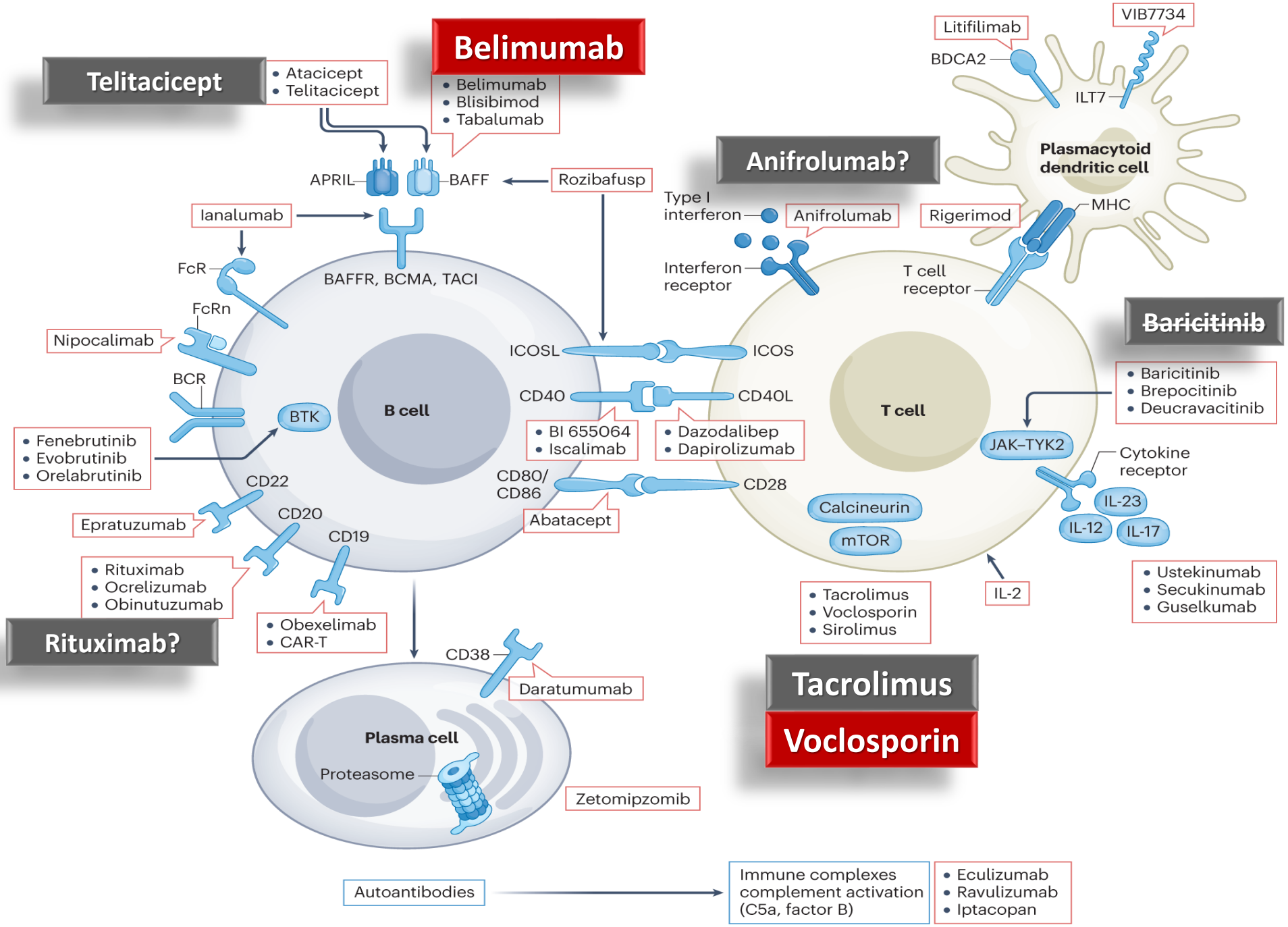
KDIGO 2021 Guideline and 2024 update: Lupus nephritis

	Standard-dose scheme	Moderate-dose scheme	Reduced-dose scheme
Methylprednisolone intravenous pulses	Nil or 0.25–0.5 g/day up to 3 days as initial treatment	0.25–0.5 g/day up to 3 days often included as initial treatment	0.25–0.5 g/day up to 3 days usually included as initial treatment
Oral prednisone equivalent (/day)			
Week 0–2	0.8–1.0 mg/kg (max 80 mg)	0.6–0.7 mg/kg (max 50 mg)	0.5–0.6 mg/kg (max 40 mg)
Week 3–4	0.6–0.7 mg/kg	0.5–0.6 mg/kg	0.3–0.4 mg/kg
Week 5–6	30 mg	20 mg	15 mg
Week 7–8	25 mg	15 mg	10 mg
Week 9–10	20 mg	12.5 mg	7.5 mg
Week 11–12	15 mg	10 mg	5 mg
Week 13–14	12.5 mg	7.5 mg	2.5 mg
Week 15–16	10 mg	7.5 mg	2.5 mg
Week 17–18	7.5 mg	5 mg	2.5 mg
Week 19–20	7.5 mg	5 mg	2.5 mg
Week 21–24	5 mg	<5 mg	2.5 mg
Week >25	<5 mg	<5 mg	<2.5 mg

Use reduced-dose steroid regime during the initial treatment of active LN when both the kidney and extrarenal disease manifestations show satisfactory improvement

Treatment of lupus nephritis:

New approaches



Mok CC et al, Nat Rev Rheumatol 2023; 19: 227–238

KDIGO 2021 Guideline and 2024 update: Lupus nephritis

2021

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 steroids plus either low-dose IV cyclophosphamide or MPAA (1B).

2024

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 steroids plus either one of the following:

- **mycophenolic acid analogues (MPAA) (1B); or**
- **low-dose intravenous cyclophosphamide (1B); or**
- **belimumab and either MPAA or low-dose IV cyclophosphamide (1B); or**
- **MPAA and a calcineurin inhibitor (CNI) when kidney function is not severely impaired** (for example eGFR ≤45 ml/min per 1.73 m^2) **(1B).**

KDIGO. Kidney Int 2021;100:S1–S276 and Kidney Int 2024; 105: 31-34

KDIGO. Kidney Int 2021;100:S1–S276 and Kidney Int 2024; 105: 31-34

KDIGO 2021 Guideline and 2024 update: Lupus nephritis

2021

Class III or IV

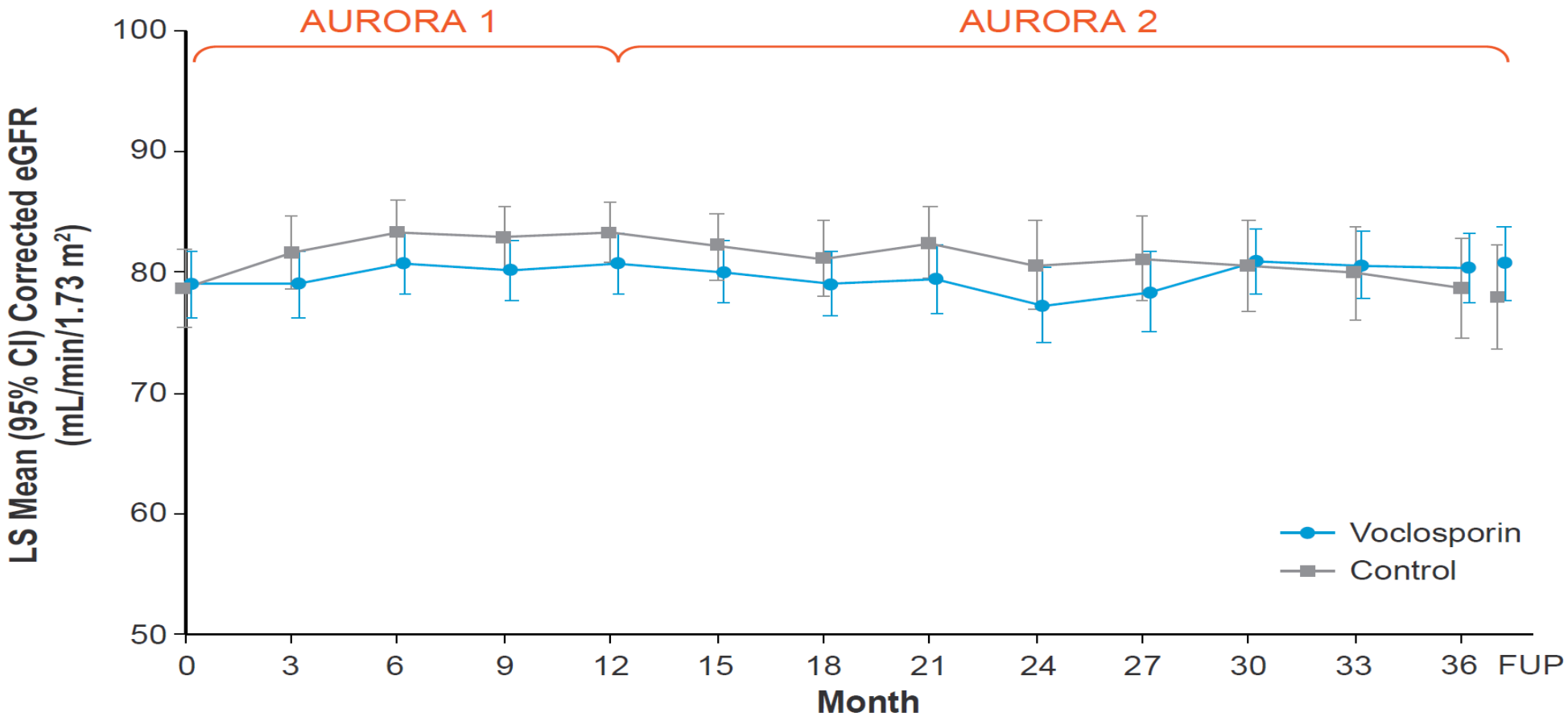
Recommendation 10.2.3.2.1. We recommend that after completion of initial therapy patients should be placed on MPAA for maintenance (1B).

Maintenance immuno-suppressive regimens	Low-dose glucocorticoids AND				
	Mycophenolic acid analogs	Azathioprine	Belimumab and mycophenolic acid analogs or azathioprine	CNI and mycophenolic acid analogs	CNI (such as voclosporin, tacrolimus or cyclosporine)
Comments 2024	Preferred treatment based on high-certainty evidence; lower flare rate than azathioprine maintenance	Low medication cost; safe in pregnancy	Efficacy and safety of belimumab demonstrated in BLISS-LN (104-wk) and open-label extension trials (28-wk) [Practice Point 10.2.3.2.5]	Efficacy and safety of voclosporin demonstrated in AURORA 1 (52-wk) and AURORA 2 continuation trials (2-yr); efficacy and safety of tacrolimus demonstrated in 'Multitarget Therapy' trial in Chinese patients in which [illegible] 24 months [Practice Point 10.2.3.2.5]	Tacrolimus and cyclosporine safe in pregnancy; insufficient pregnancy data on voclosporin

Preferred

Continue in maintenance if good response initially

Voclosporin – AURORA 1 and 2 Phase III Trials: eGFR



Voclosporin (n)	116	116	116	116	116	114	114	109	103	102	99	100	100	96
Control (n)	100	100	100	100	100	98	96	90	81	84	85	84	87	85

CI, confidence interval; eGFR, estimated glomerular filtration rate; FUP, follow-up (occurred 4 weeks after study drug was discontinued); LS Mean, least squares mean. Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². Analysis of AURORA 2 patients includes data from pre-treatment baseline of AURORA 1, 12 months in AURORA 1 and up to 25 months in AURORA 2. Error bars represent 95% CI.

Voclosporin – AURORA 1 and 2 Phase III Trials: Adverse Events

	Control, n (%)			Voclosporin, n (%)		
	Year 1 n=100	Year 2 n=100	Year 3 n=85	Year 1 n=116	Year 2 n=116	Year 3 n=103
Adverse Events (AE), n (%)	84 (84.0)	66 (66.0)	46 (54.1)	103 (88.8)	85 (73.3)	67 (65.0)
Serious AEs, n (%)	13 (13.0)	18 (18.0)	8 (9.4)	13 (11.2)	13 (11.2)	8 (7.8)
Selected AEs, n (%)						
Infections and Infestations	60 (60.0)	30 (30.0)	21 (24.7)	70 (60.3)	45 (38.8)	35 (34.0)
Coronavirus infection	0	2 (2.0)	11 (12.9)	0	2 (1.7)	5 (4.9)
Headache	7 (7.0)	3 (3.0)	2 (2.4)	22 (19.0)	6 (5.2)	2 (1.9)
Tremor	0	0	0	4 (3.4)	0	0
Hyperglycemia	0	0	0	0	1 (0.9)	0
Hypertension	6 (6.0)	5 (5.0)	2 (2.4)	24 (20.7)	7 (6.0)	3 (2.9)
eGFR Decreased	6 (6.0)	3 (3.0)	2 (2.4)	22 (19.0)	10 (8.6)	4 (3.9)
Renal Impairment	1 (1.0)	1 (1.0)	1 (1.2)	5 (4.3)	3 (2.6)	0
Acute Kidney Injury	0	0	0	3 (2.6)	0	0
Neoplasms Benign, Malignant and Unspecified AEs	2 (2.0)	0	2 (2.4)	2 (1.7)	1 (0.9)	1 (1.0)

Teng Y.K. et al., 59th European Renal Association (ERA) Congress 2022. Abstract FC 054. Rovin BH et al. Lancet. 2021;397:2070. Personal communication with Prof. Floege

Voclosporin – AURORA 2 Phase III Trial: Renal Flares

	Control n=100	Voclosporin n=116
Adequate response, % (n/n)	**73%** (73/100)	**87%** (101/116)
Renal flare in patients with prior adequate response % (n/n)	**26%** (19/73)	**24%** (24/101)
Odds ratio vs control (95% CI)		0.85 (0.42, 1.73)
p-value		0.662

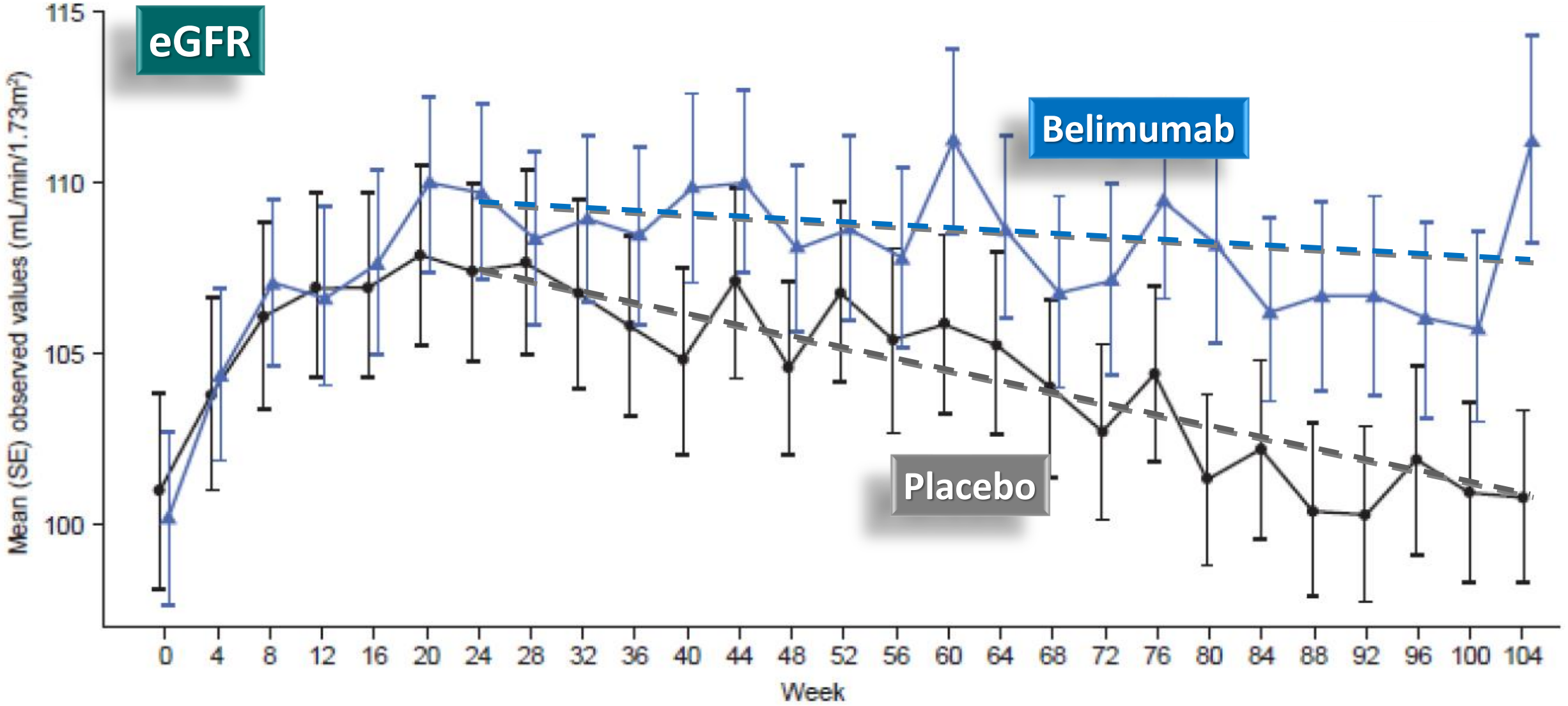
Adequate response: A sustained reduction in UPCR to ≤0.7 mg/mg.

Renal flare: increase to UPCR >1 mg/mg from a post-response baseline of <0.2 mg/mg, or an increase to UPCR >2 mg/mg from a post-response baseline between 0.2 to 1.0 mg/mg, or a doubling of UPCR for pretreatment baseline values of UPCR >1 mg/mg.

Teng Y.K. et al., 59th European Renal Association (ERA) Congress 2022. Abstract FC 054. Personal communication with Prof. Floege

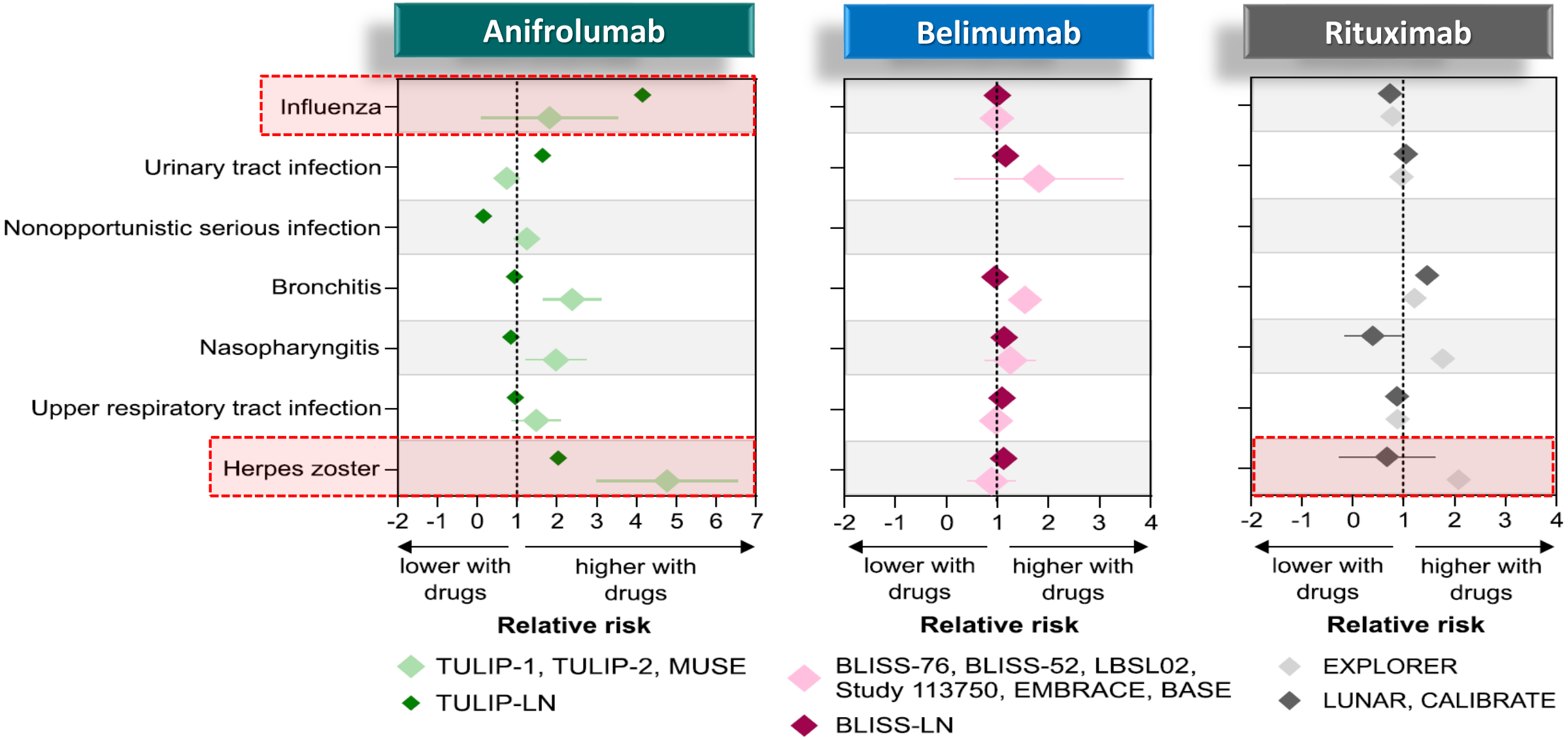
Furie R et al, NEJM 2020; 383: 1117-28

BLISS-LN trial: belimumab in lupus nephritis



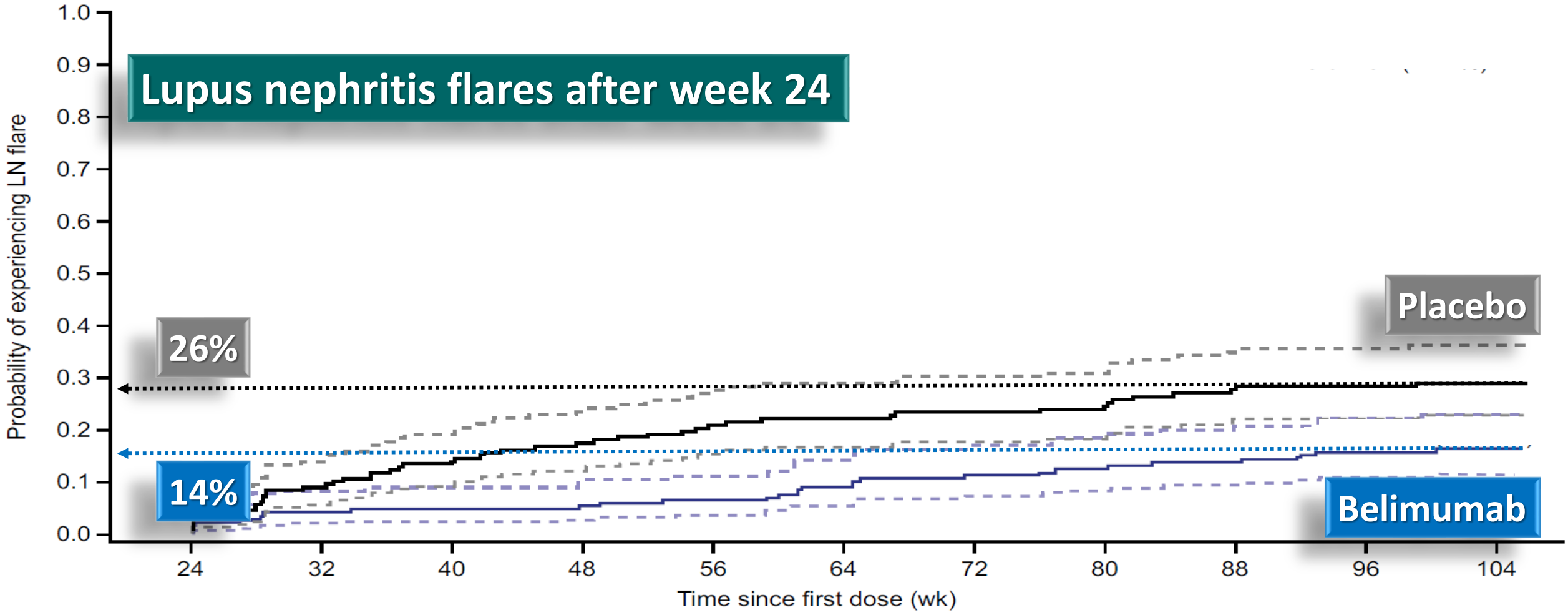
Steiger S et al, Front Immunol 2022, DOI 10.33897fimmu.2022.999704

Infectious complications with different new biologics in lupus nephritis



Rovin BH et al, Kidney Int 2022; 101: 403-13

BLISS-LN trial: belimumab in lupus nephritis



Number of patients at risk

Placebo	196	167	154	142	133	131	127	124	117	115	68
Belimumab	194	175	167	164	161	153	144	139	134	130	93

The influence of repeated flares in response to therapy and prognosis in lupus nephritis

Background

Repeated lupus nephritis flares have been associated with worse long term kidney function.

Methods

LN cohort (2008–2018) N=441

- 1st LN flare
- 2nd LN flare
- 3rd LN flare

Endpoints

- Response to therapy
- Renal relapses
- Progression of kidney disease
- Patient survival

Results

	Complete response	Partial response	↓30% eGFR	Patient mortality
1st	Reference	Reference	Reference	Reference
2nd	↓31%	↓31%	↑50%	↑93%
3rd	↓62%	↓40%	↑69%	↑285%

Conclusion

A progressive number of LN flares is associated with lower response to therapy, higher rates of progression of kidney disease, and lower patient survival.

NEPHROLOGY DIALYSIS TRANSPLANTATION

Pérez-Arias, A.A., et al. NDT (2022)
@NDTSocial

Summary of important differences: Voclosporin vs. Belimumab

Voclosporine	Belimumab
Use cautiously if GFR is impaired (e.g., <45 ml/min per 1.73 m^2)	May be used if GFR is at least 30 ml/min per 1.73 m^2; may slow decline of GFR[a]
Use cautiously if widespread sclerotic and/or fibrotic changes are present	Not determined
Effective at any level of proteinuria; may be especially effective in patients with severe proteinuria with significant podocyte damage	More effective in patients with proteinuria <3 g/d
No effect on flare rate	May decrease rate of severe flares
Was not tested in combination with cyclophosphamide	Effective in combination with MMF; uncertain effectiveness in combination with cyclophosphamide
Oral only	Intravenous/subcutaneous
Efficacy in extrarenal lupus to be determined	Long track record of efficacy in extrarenal lupus
Add-on therapy did not increase the incidence of adverse events; monitor acute eGFR variations with voclosporin	Add-on therapy did not increase the incidence of adverse events
Pregnancy: Use not recommended (consider tacrolimus)	Use not recommended

Kidney Int 2024; 105: 31-34

ANCA-associated vasculitis

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KDIGO executive conclusions

Executive summary of the KDIGO 2024 Clinical Practice Guideline for the Management of ANCA–Associated Vasculitis

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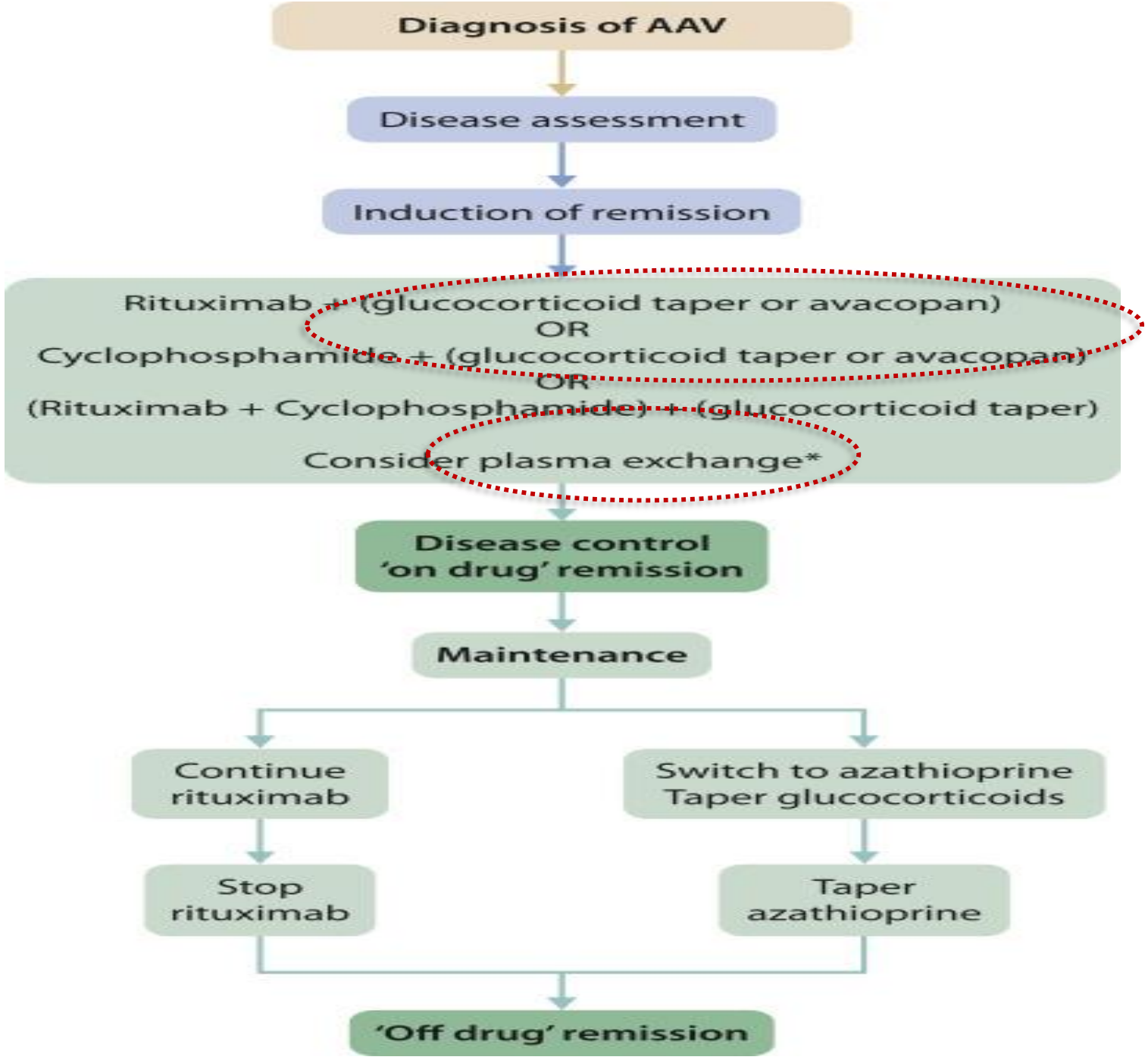
Jürgen Floege[1], David R.W. Jayne[2], Jan-Stephan F. Sanders[3], Vladimír Tesar[4], Ethan M. Balk[5], Craig E. Gordon[6], Gaelen Adam[5], Marcello A. Tonelli[7], Michael Cheung[8], Amy Earley[8] and Brad H. Rovin[9]

[1]Division of Nephrology, University Hospital, Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen, Aachen, Germany; [2]Division of Experimental Medicine & Immunotherapeutics, School of Clinical Medicine, University of Cambridge, Cambridge, UK; [3]Division of Nephrology, Department of Internal Medicine, University of Groningen, Groningen, The Netherlands; [4]Department of Nephrology, 1st Faculty of Medicine and General University Hospital, Charles University, Prague, Czech Republic; [5]Center for Evidence Synthesis in Health, Brown University School of Public Health, Providence, Rhode Island, USA; [6]Division of Nephrology, Tufts Medical Center, Boston, Massachusetts, USA; [7]Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; [8]KDIGO, Brussels, Belgium; and [9]Department of Internal Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA

Kidney International (2024) **105,** 447–449

KDIGO 2021 Guideline and 2024 update:

ANCA-associated vasculitis



Floege J et al,
Corrigendum to
Kidney Int. 2024;105(3S):S71–S116

Floege J et al, Kidney Int. 2024;105(3S):S71–S116

KDIGO 2021 Guideline and 2024 update: ANCA associated vasculitis

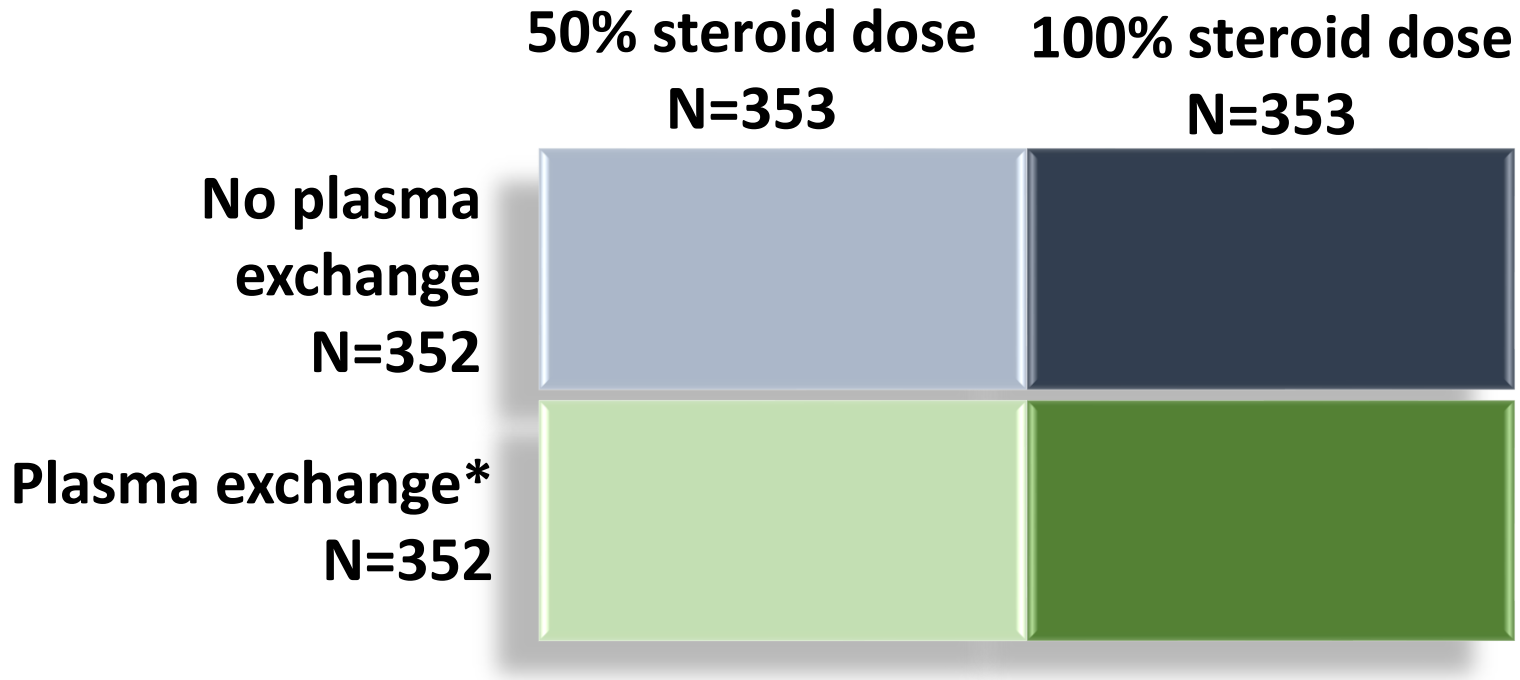
Recommendation 9.3.1.1 "We recommend that glucocorticoids in combination with cyclophosphamide or rituximab be used as initial treatment of new-onset AAV (1B)"

no change, but the discussion now places stronger emphasis on a more rapid reduction of glucocorticoid dose based on the recent LoVAS study => 0.5 mg/kg/d prednisolone starting dose (Furuta S et al, JAMA 2021)

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

Pexivas: Plasmapheresis in severe ANCA vasculitis

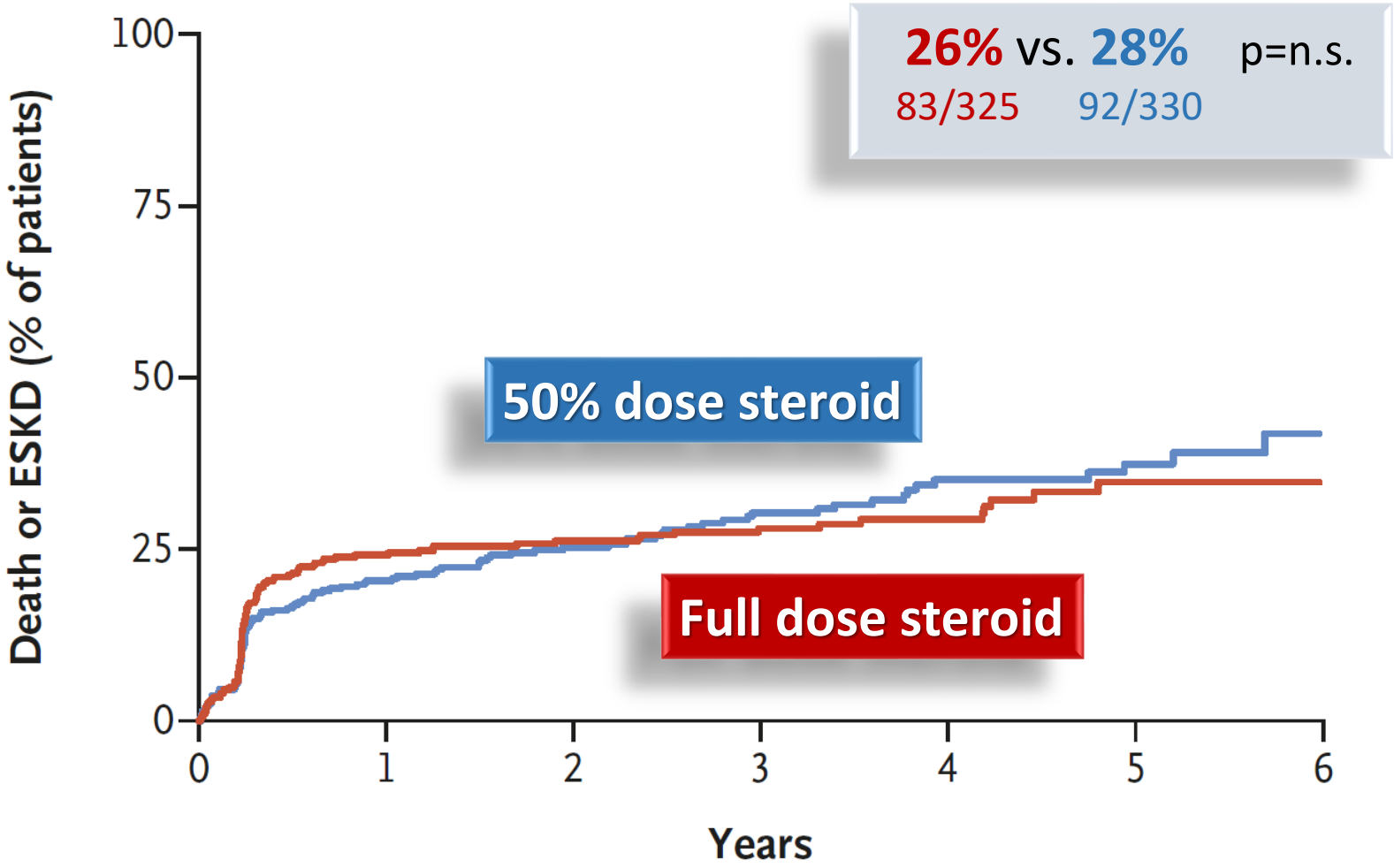
- 704 patients
- 18% pulmonary hemorrhage, 9% severe
- Median s-creatinine 327 µmol/l, 20% dialysis dependent



* 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



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		

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

Mimura N et al. RMD Open 2023; 9:e002787. Doi:10.1136/rmdopen-2022-002787

Prevalence and Risk Factors for Aseptic Necrosis of the Femoral Head in Patients with ANCA Vasculitis

186 AAV-Patients, MRT hips > 6 months after initial remission induction therapy

Table 2 Stage and type distribution of osteonecrosis of the femoral head in ANCA-associated vasculitis patients†

A. Overall necrotic joints (Total n=54 from 33 patients with ONFH)		Type, n			
		A	B	C-1	C-2
Stage, n	1	8	7	11	4
	2	1	2	6	2
	3A	0	0	1	5
	3B	0	0	1	4
	4	0			

17%

76% pre-collapse stage

24% collapse stage

56% of precollapse at risk of collapse

- **17% o AAV patients with hip necrosis upon screening!!!**
- **Prednisolone-dose on day 90 = independent risk factor** (but not steroid pulses, initiale or cumulativedose)
- **ROC-Analysis: cut-off dose = 20 mg/d**

Table 3 Independent risk factor of osteone

Logistic regression (forced entry) Univariate predictors†			
Prednisolone dose on day 90, median (IQR), mg/day	1.072	1.017 to 1.130	0.009
Rituximab use	0.592	0.239 to 1.465	0.257

Floege J et al, Corrigendum to Kidney Int. 2024;105(3S):S71–S116

KDIGO 2021 Guideline and 2024 update: ANCA associated vasculitis

Induction Therapy

Rituximab preferred	Cyclophosphamide preferred
• Children and adolescents • Pre-menopausal women and men concerned about their fertility • Frail older adults • Glucocorticoid-sparing especially important • Relapsing disease • PR3–ANCA disease	• Rituximab difficult to access • Severe GN (SCr >4 mg/dl [354 µmol/l])*

Maintenance

Rituximab preferred	Azathioprine preferred
• Relapsing disease • PR3–ANCA disease • Frail older adults • Glucocorticoid-sparing especially important • Azathioprine allergy	• Low baseline IgG (<300 mg/dl) • Limited availability of rituximab

Vassilopoulos A et al, Front Med 2023; doi: 10.3389/fmed.2023.1110548

Cumulative incidence of serious infections in patients with ANCA vasculitis and maintenance immunosuppression – a meta-analysis

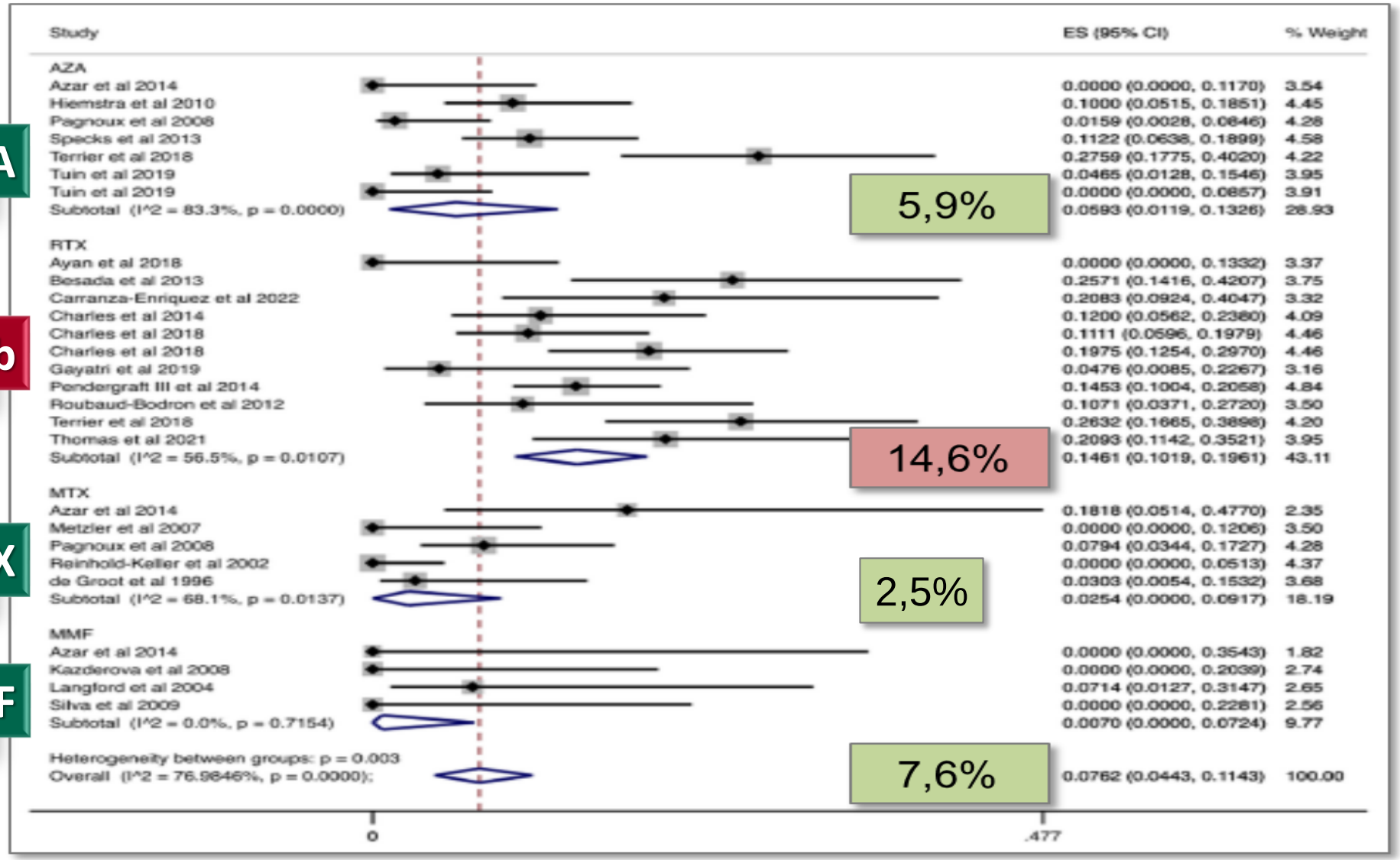
21 Studies
1284 patients

AZA

Rituximab

MTX

MMF



Floege J et al, Kidney Int. 2024;105(3S):S71–S116

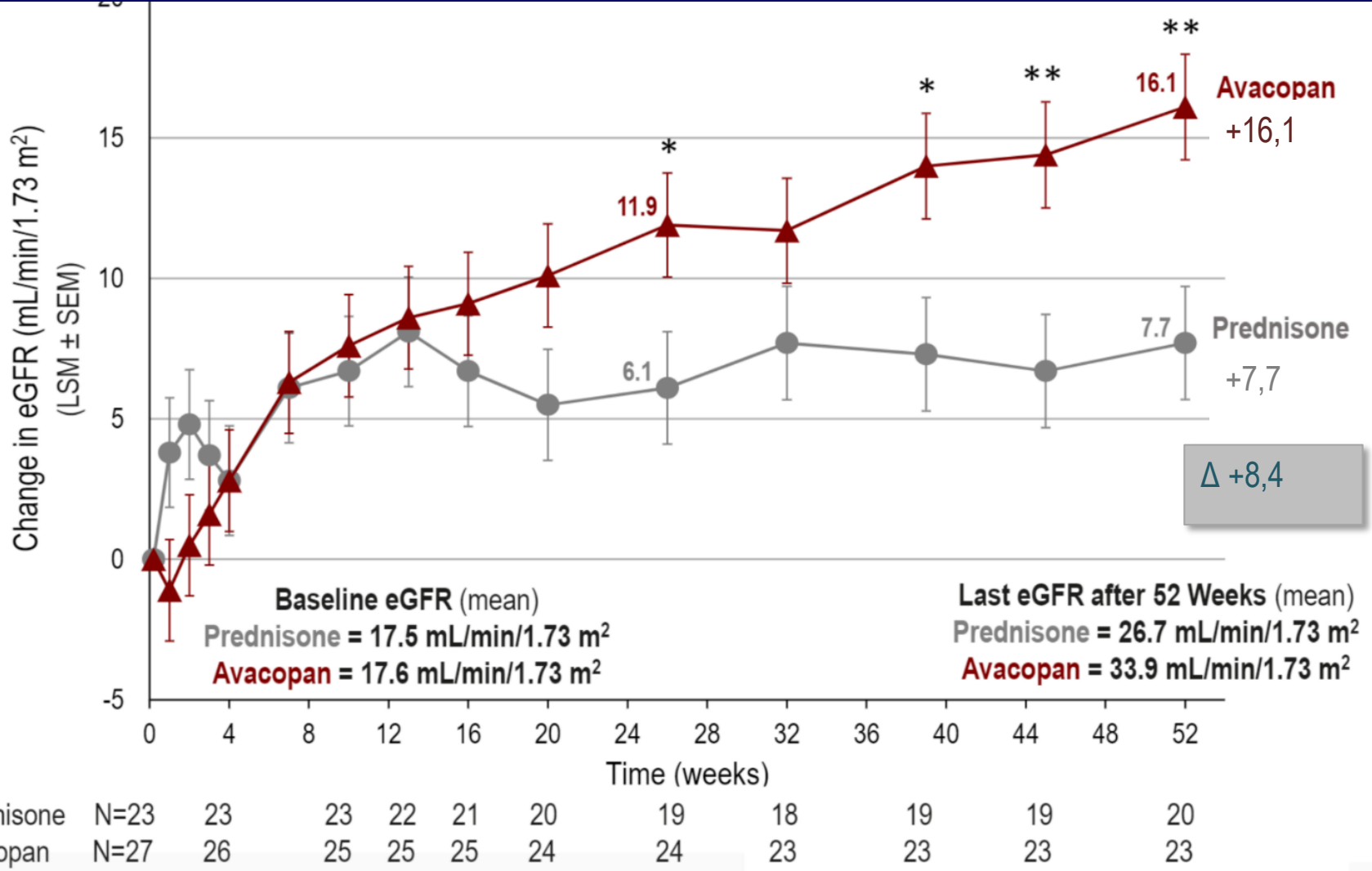
KDIGO 2021 Guideline and 2024 update: ANCA associated vasculitis

Recommendation 9.3.1.1 "We recommend that glucocorticoids in combination with cyclophosphamide or rituximab be used as initial treatment of new-onset AAV (1B)"
no change, but the discussion now places stronger emphasis on a more rapid reduction of glucocorticoid dose based on the recent LoVAS study => 0.5 mg/kg/d prednisolone starting dose (Furuta S et al, JAMA 2021)

Practice Point 9.3.1.7: Avacopan may be used as an alternative to glucocorticoids.
Patients with an increased risk of glucocorticoids toxicity are likely to have the most benefit from avacopan. Patients with lower GFR may benefit from greater GFR recovery.

Cortazar FB et al. Kidney Int Reports 2023; 8:860-870

Recovery of GFR with avacopan in AAV patients with baseline eGFR <20 ml/min – ADVOCATE trial



- One patient's eGFR in the **avacopan** group increased to **65 mL/min/1.73 m²** (baseline: **17 mL/min/1.73 m²**)

LSM = least squares mean; SEM = standard error of mean

*p<0.05, **p<0.01 by mixed effects models for repeated measures (MMRM) with treatment group, visit, treatment-by-visit interaction, and randomization strata as factors and baseline as covariate

Floege J et al, Kidney Int. 2024;105(3S):S71–S116

KDIGO 2021 Guideline and 2024 update: ANCA associated vasculitis

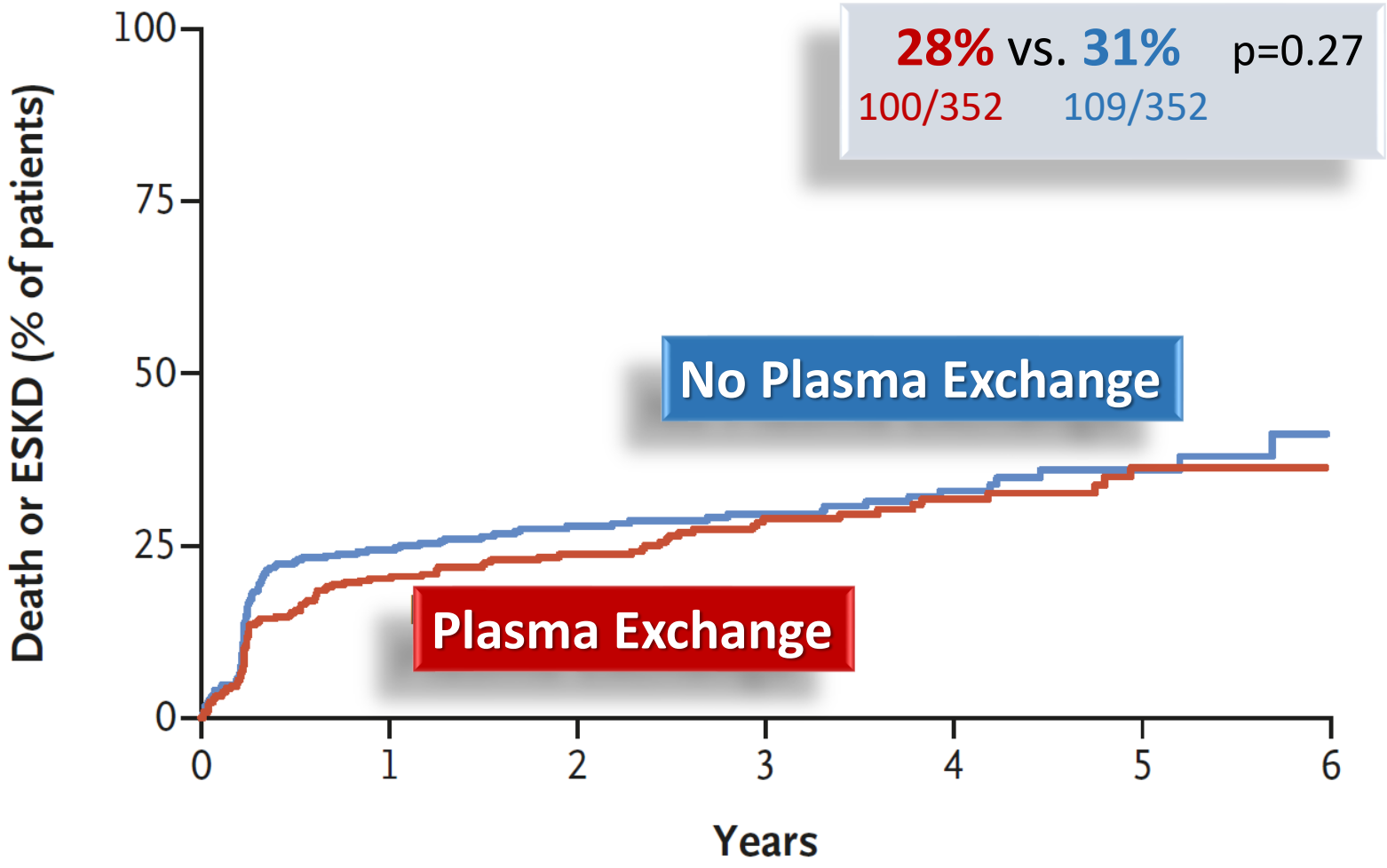
Recommendation 9.3.1.1 "We recommend that glucocorticoids in combination with cyclophosphamide or rituximab be used as initial treatment of new-onset AAV (1B)" no change, but the discussion now places stronger emphasis on a more rapid reduction of glucocorticoid dose based on the recent LoVAS study => 0.5 mg/kg/d prednisolone starting dose (Furuta S et al, JAMA 2021)

Practice Point 9.3.1.7: Avacopan may be used as an alternative to glucocorticoids. Patients with an increased risk of glucocorticoids toxicity are likely to have the most benefit from avacopan. Patients with lower GFR may benefit from greater GFR recovery.

Practice Point Practice Point 9.3.1.9: Consider plasma exchange for patients with SCr >3.4 mg/dl (>300 mmol/l), patients requiring dialysis or with rapidly increasing SCr, or patients with diffuse alveolar hemorrhage who have hypoxemia.

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

Pexivas: Plasmapheresis in severe ANCA vasculitis



More work in progress

- **IgA nephropathy** (end of 2024)
- **Nephrotic syndrome in children** (autumn 2024)
- **Membranous nephropathy**