SUPPLEMENTARY MATERIALS 7: Dosing Concerns

2024 American College of Rheumatology (ACR) Guideline for the Screening, Treatment, and Management of Lupus Nephritis

Medication Dosing: Adjustment Suggestions

Medication	eGFR 30-60	eGFR < 30	ESKD / Dialysis	Comments
Hydroxychloroquine	No change	Reduce dose by 25%*	Reduce dose by 25%*	Limited data on precise dose reduction for lowered eGFR; however, CKD is a risk factor for ocular toxicity. Drug levels are available.
RAAS-I: ACE-I and ARB	No specific recommendations for dosage adjustment unless change in eGFR and/or K+		Use alternate therapy unless benefit for CVD outweighs risk	Monitor eGFR and K+: Some fall in eGFR is expected and tolerable if stabilization at <20% of baseline eGFR. If eGFR does not stabilize and/or falls more than 20% of baseline, or if elevated K+, decrease dose and recheck eGFR within 2 weeks.
Glucocorticoids	No dosage adjustment			
Cyclophosphamide	No change	50-75% usual dose if high dose monthly regimen	50% usual dose if high dose monthly regimen	Monitor white blood cell count/differential and urinalysis.
Mycophenolic acid analogs	No change	Limit dose to MMF/ equivalent 2 g/day	Limit dose to MMF/ equivalent 2 g/day	Note: MMF 1 g = MPA 720 mg Drug levels are available.
Azathioprine	No change	50-100% usual dose	50-100% Usual dose	Important non-kidney concerns. Hepatic metabolism issues: adjust dose even with good kidney function. Hepatic enzymes TPMT or NUDT15: Intermediate metabolizer: 30-80% usual dose

				Poor metabolizer: Consider alternative therapy. Concomitant allopurinol: Reduce dose to 25-33% usual. Do not use with febuxostat.
CNI:				
Voclosporin	Use if eGFR >45	Use if eGFR >45 Modification for lowered eGFR while on therapy provided in package label.**		Patients with CrCl ≤45 excluded from clinical trials, do not recommend use unless benefit clearly outweighs risk. Monitor eGFR and adjust as indicated. **
Tacrolimus, Cyclosporine	No dosage adjustment specified on drug labels (no FDA approval for LN)			Monitor eGFR: Some fall in eGFR is expected and tolerable if stabilization at <20% of baseline eGFR. If eGFR does not stabilize and/or falls more than 20% of baseline, decrease dose and recheck eGFR within 2 weeks. Consider drug levels.
Belimumab	No dosage adjustment			
Rituximab	No dosage adjustment			Urinary losses and altered pharmacodynamics reported in patients with nephrotic range proteinuria but implications for dosing are uncertain. For patients with high levels of proteinuria, some experts suggest checking peripheral B cell counts 1-2 weeks after the last rituximab infusion. If B cell depletion has not been achieved, might consider giving an additional dose of rituximab.

General comments:

- Avoid nonsteroidal anti-inflammatory drugs (NSAIDs) and other nephrotoxins.
- Start at the low end of the recommended range where lower medication doses are recommended and titrate up to the desired effect (e.g., reduction in proteinuria, control of blood pressure) while monitoring for toxicity and adverse events such as eGFR decline.
- Consider drug/metabolite levels (when available) if indicated to guide therapy, avoid over- or under-dosing, or rule out non-adherence.

Abbreviations:
ACE-I: Angiotensin converting enzyme inhibitors
ARB: Angiotensin II receptor blockers
CNI: Calcineurin inhibitor therapies
CVD: Cardiovascular disease
eGFR: Estimated glomerular filtration rate
K+: Potassium (serum)
MMF: Mycophenolate mofetil
MPA: Mycophenolic acid
RAAS-I: Renin-angiotensin-aldosterone system inhibitors

This table represents a synthesis of various published sources as well as the expert opinion of Lupus Nephritis Guideline Team members. Most references do not specify specific changes in dose; as a result, these are dose adjustment and monitoring suggestions only.
Sources:
KDIGO Lupus nephritis management clinical practice guideline*
UpToDate Lexidrug (accessed 9/12/2024)
FDA drug labels (accessed 9/12/2024) including voclosporin**
*Rovin BH, Ayoub IM, Chan et al. KDIGO 2024 Clinical Practice Guideline for the management of LUPUS NEPHRITIS. Kidney International. 2024 Jan 1;105(1):S1-69.
** https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213716s004lbl.pdf#page=25 (accessed 9/12/2024). Voclosporin package label: modify dosage based on eGFR change. If eGFR <60 and reduced from baseline by >20% and <30%, reduce dose by 7.9 mg BID. Reassess eGFR within 2 weeks; if eGFR still reduced from baseline by >20%, reduce dose again by 7.9 mg BID. If eGFR <60 and reduced from baseline by ≥30%, discontinue. Reassess eGFR within 2 weeks; consider re-initiating at a lower dose (7.9 mg BID) only if eGFR has returned to ≥80% of baseline. For patients that had a decrease in dose due to eGFR, consider increasing the dose by 7.9 mg twice a day for each eGFR measurement that is ≥80% of baseline; do not exceed the starting dose.