

Evaluation and Management of Suspected Immune-Mediated Nephritis

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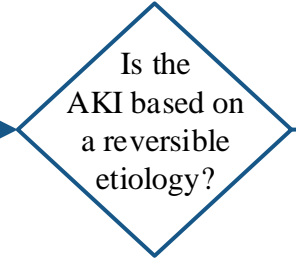
PRESENTATION

ASSESSMENT

TREATMENT

Patient presents with increased serum creatinine (SCr)¹ after immune checkpoint inhibitor (ICI) initiation and up to 12 months after last dose of immunotherapy²

- Laboratory evaluation: CBC with differential, basic metabolic panel (BMP), cytokine 3 assay, urinalysis (UA), urine electrolytes, spot protein to creatinine ratio, urine eosinophils
- Consider reversible etiologies of AKI
 - Pre-renal/obstruction: check for presence of foley and obtain renal ultrasound
 - Infection/sepsis
 - Presence of nephrotoxins: previous history of antibiotics, IV contrast, NSAID and/or PPI use, current nephrotoxic chemotherapies



Yes
No

Initiate appropriate treatments based on determined reversible etiology

- Hold immunotherapy and order the following:
- Nephrology consult/referral
 - Laboratory evaluation:
 - Inpatient: Daily BUN, SCr, and electrolytes
 - Outpatient: Weekly BUN, SCr, and electrolytes
 - If hematuria and/or proteinuria present, consider ICI-induced etiologies such as vasculitis and glomerulonephritis by checking the following serologies, in addition to obtaining a kidney biopsy: ANA, double stranded DNA, RF, C3, C4, ANCA, anti-GBM, hepatitis B and C, HIV, RPR, SPEP, UPEP, IFE

Treatment based on immune-mediated AKI grading¹, see [Page 2](#)

AKI = acute kidney injury
 ANA = antinuclear antibody
 ANCA = antineutrophil cytoplasmic antibodies
 Anti-GBM = anti-glomerular basement membrane
 C3 = complement component 3
 C4 = complement component 4
 NSAID = nonsteroidal anti-inflammatory drugs

PPI = proton pump inhibitor
 RF = rheumatoid factor
 RPR = rapid plasma reagin
 SPEP = serum protein electrophoresis
 UPEP = urine protein electrophoresis
 IFE = immunofixation electrophoresis

¹ Refer to AKI grading chart, see [Appendix A](#)

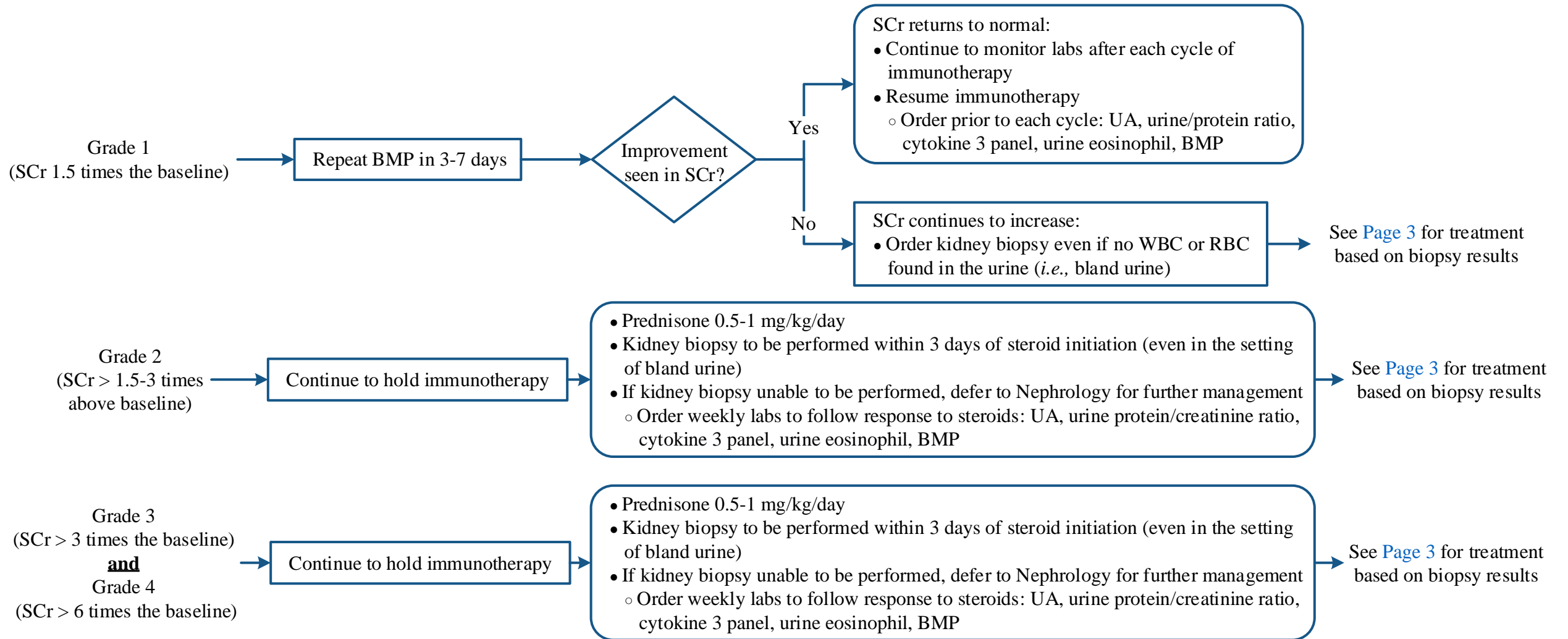
² PD-1 inhibitors (pembrolizumab, nivolumab, cemiplimab), PD-L1 inhibitors (atezolizumab, avelumab, durvalumab), CTLA-4 inhibitor (ipilimumab)

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IMMUNE-MEDIATED AKI GRADE¹

TREATMENT



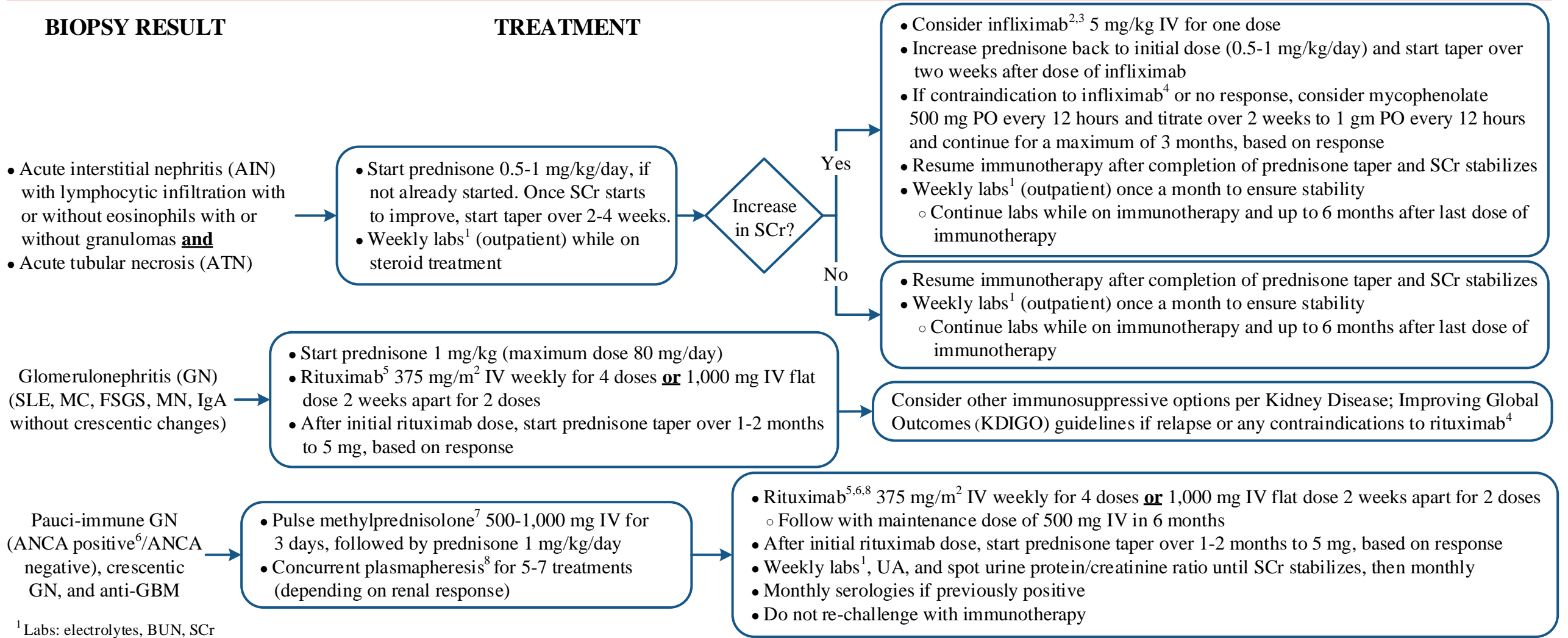
anti-VEGF = anti-vascular endothelial growth factor

¹ Refer to AKI grading chart, see [Appendix A](#)

Note: Evaluate the risks and benefits of a kidney biopsy with the patient and the oncology team, especially with patients with a solitary kidney. In addition, coordinate with the oncology team if the patient is on anti-VEGF treatments and/or anticoagulation to be held prior to the biopsy to decrease the risk of bleeding.

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¹ Labs: electrolytes, BUN, SCr

² Follow TNF-alpha every 2 weeks if it coincides with creatinine elevation after initial dose; can re-dose in 2-4 weeks

³ Screening tests to be performed prior to starting infliximab: quantiFERON-TB gold (QFT-GIT) or T-SPOT TB test to screen for TB exposure and hepatitis B panel. Consider screening for fungal infections, if indicated.

⁴ See Appendix B for Contraindications to Infliximab or Rituximab

⁵ Check hepatitis B panel to rule out exposure to hepatitis B; consult/refer to Infectious Diseases if hepatitis B panel shows prior exposure. Start PCP prophylaxis for patients on high dose steroids and starting rituximab; avoid sulfamethoxazole/trimethoprim as an option.

⁶ Follow Anti-PLA2R if positive for response and ANCA serologies if positive

⁷ If already on prednisone, switch to methylprednisolone after biopsy confirmation

⁸ Hold plasmapheresis after rituximab dose to avoid removal of drug

ANCA = antineutrophil cytoplasmic antibodies
 FSGS = focal segmental glomerulosclerosis
 MC = minimal change disease
 MN = membranous nephropathy
 SLE = systemic lupus erythematosus

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APPENDIX A: Grades of Immune-Mediated AKI

Determine Grade (G) of AKI

- Grade 1 (G1): creatinine 1.5 times the baseline
- Grade 2 (G2): creatinine > 1.5-3 times above the baseline
- Grade 3 (G3): creatinine > 3 times the baseline
- Grade 4 (G4): creatinine > 6 times the baseline

APPENDIX B: Contraindications to Infliximab and Rituximab

Contraindications to infliximab

- Tuberculosis exposure
- Hepatic impairment
- Heart failure

Contraindication to rituximab

- Hepatitis B exposure

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SUGGESTED READINGS

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DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the Nephritis experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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