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Adaptation to New Guidelines of Management for ANCA Associated GN

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Antineutrophil cytoplasmic antibody–associated vasculitis (AAV) is a life-threatening condition often causing rapidly progressive glomerulonephritis and multi-organ damage. The Kidney Disease: Improving Global Outcomes (KDIGO) 2021 Glomerular Diseases guideline provided comprehensive recommendations for AAV management. However, new therapeutic developments – notably the approval of avacopan, an oral complement 5a receptor antagonist, in late 2021 – and emerging evidence on safer induction regimens prompted a focused 2024 update. The rationale for updating the KDIGO guidelines includes incorporating avacopan as a steroid-sparing option and refining induction strategies based on recent clinical trials. The 2024 KDIGO update introduces significant changes in AAV induction therapy. First, immunosuppressive induction priority now emphasizes rituximab over cyclophosphamide as first-line, reflecting trials showing comparable efficacy with less toxicity. Cyclophosphamide remains an option, particularly for severe presentations, and in the most aggressive cases, a combination of rituximab plus cyclophosphamide can be considered. Second, the glucocorticoid (GC) strategy has shifted toward minimization. The new guideline supports lower initial steroid doses and faster tapering, informed by evidence that reduced-dose regimens are noninferior to high-dose regimens for remission induction and yield fewer infections. Third, avacopan is now recommended as an alternative to traditional GC in induction. Avacopan can replace or substantially reduce GC exposure in appropriate patients. The guideline highlights explicitly avacopan's utility in patients at high risk for steroid-related toxicity and those with severe renal impairment, as data suggest greater GFR recovery with avacopan than with high-dose steroids. Fourth, indications for adjunct plasma exchange have been narrowed. Whereas 2021 guidance suggested plasma exchange for very advanced renal disease (creatinine >5.7 mg/dL) or life-threatening pulmonary hemorrhage, the 2024 update raises caution: plasma exchange is now only considered in extreme cases such as dialysis-dependent renal failure (creatinine >3.4 mg/dL) or diffuse alveolar hemorrhage with hypoxemia. The 2024 KDIGO AAV guideline

update reflects a paradigm shift toward remission induction with less glucocorticoid exposure and more targeted therapy. For nephrologists, the key takeaways are the endorsement of rituximab-based induction whenever feasible, the option to replace prolonged high-dose steroids with avacopan in suitable patients, and a more restricted use of plasma exchange. Incorporating avacopan into induction regimens offers the dual benefits of effective disease control and mitigation of steroid-related toxicity.

Keywords: ANCA associated vasculitis, glomerulonephritis, glucocorticoid, rituximab, avacopan