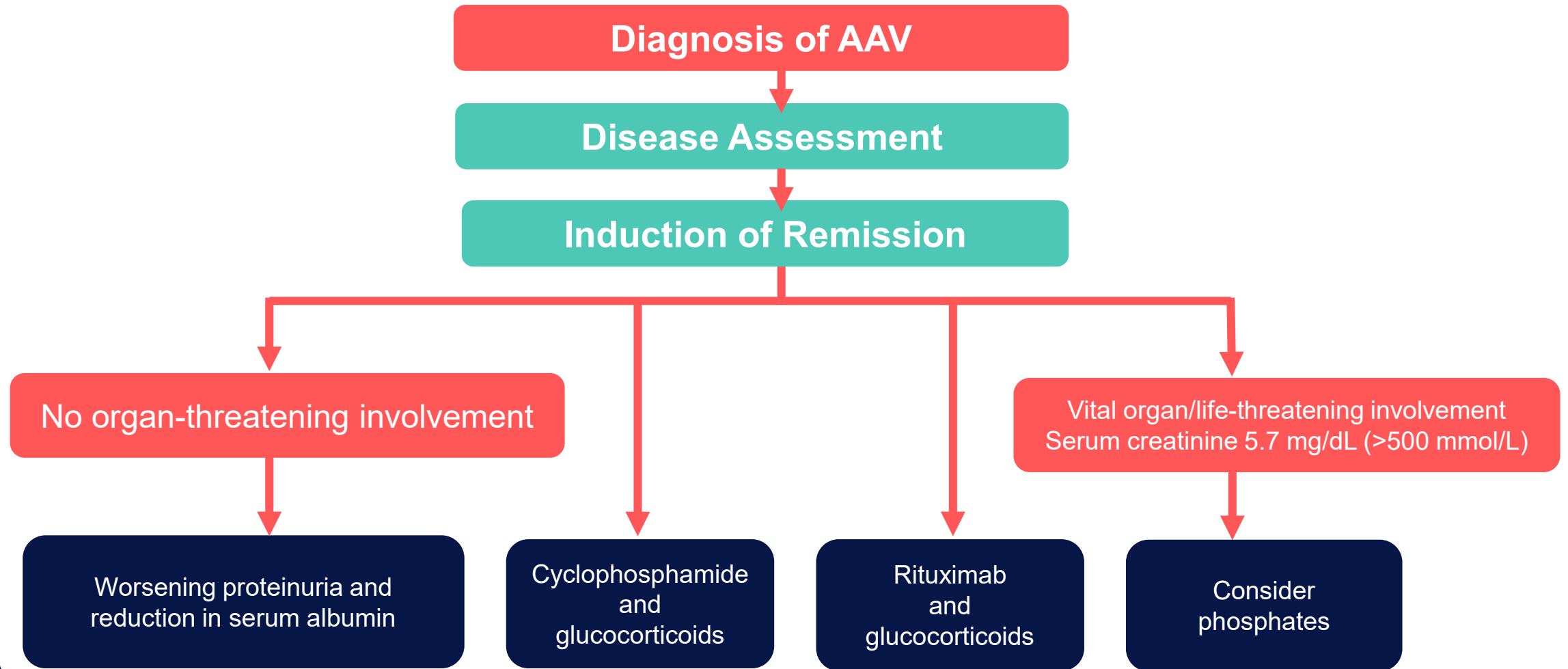


# KDIGO: Recommendations in AAV



# AAV Treatment Comparison and Selection

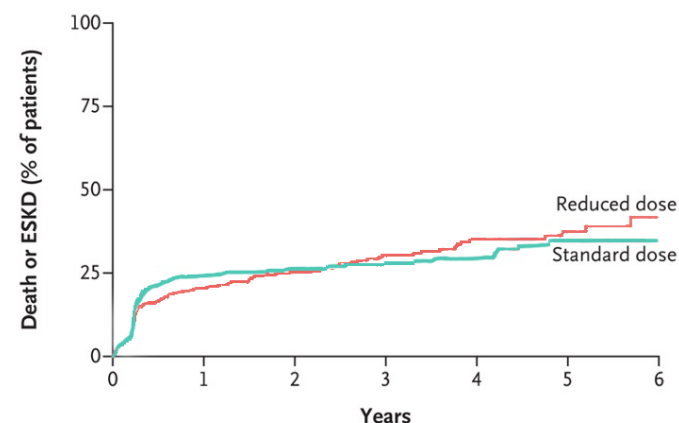
Rituximab preferred	Cyclophosphamide preferred
<ul style="list-style-type: none"><li>• Children and adolescents</li><li>• <b>Premenopausal women and men concerned about fertility</b></li><li>• Frail older adults</li><li>• Glucocorticoid-sparing especially important</li><li>• Relapsing disease</li><li>• PR3-ANCA disease</li></ul>	<ul style="list-style-type: none"><li>• Rituximab difficult to access</li><li>• Severe GN (SCr &gt; 4 mg/dL [35 mmol/L]), combination of 2 IV pulses of cyclophosphamide with rituximab can be considered</li></ul>

Hypogammaglobulinemia  
Late-onset neutropenia } Infection risk ↑



# PEXIVAS Randomized Controlled Trial

- Conclusions
  - **Reduced exposure to oral glucocorticoids** was noninferior to a standard-dose regimen with respect to the risk of death or ESKD
  - **Risk of serious infections** at  $\leq 1$  year less common with reduced-dose corticosteroids



No. at Risk	0	1	2	3	4	5	6
Reduced dose	353	256	185	133	80	48	9
Standard dose	351	240	184	138	84	39	11

## Results: Steroids – Secondary Outcomes

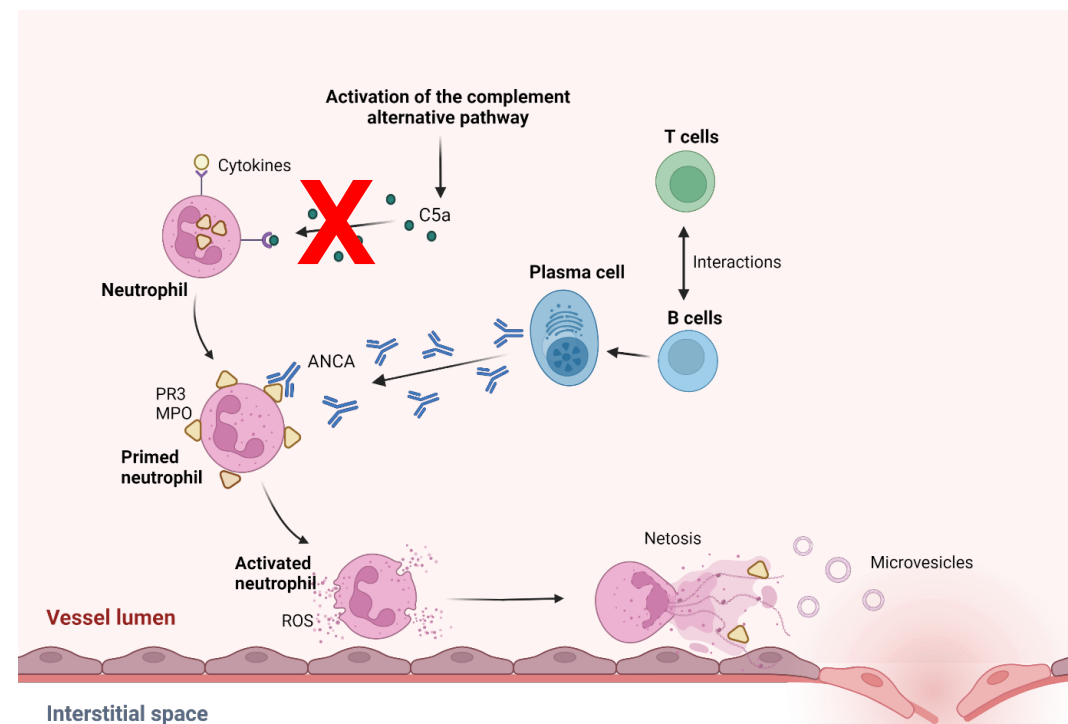
Outcome	Reduced	Standard	Hazard Ratio (95% CI)	P-value
Death, n (%)	46 (13)	53 (15)	0.78 (0.53 – 1.17)	0.23
ESRD, n (%)	70 (20)	68 (19)	0.96 (0.68 – 1.34)	0.65
Sustained Remission, n (%)	204 (58)	193 (55)	1.04 (0.92 – 1.19)	0.48
SAEs, n (%)	231 (65)	218 (62)	1.05 (0.94 – 1.17)	0.20
<b>Incidence Rate Ratio (95% CI)</b>				
Year 1 Serious Infections, n (%)	96 (27)	116 (33)	0.69 (0.52 – 0.93)	0.02

The cumulative GC dose was 40% of that in a standard dose regimen group at 6 months



# C5a Inhibition in ANCA Vasculitis

- **Alternative complement pathway:** critical role in the pathogenesis
- **C5a inhibitors:**
  - Antagonize C5a receptors to block C5a-mediated **neutrophil activation and migration**



Pathways in the pathogenesis of AAV. Adapted from "Endothelial Barrier Inflammation and Leak (Layout)," by Biorender.com (2022). Retrieved from <https://app.biorender.com/biorender-templates>; courtesy Asta Jonasdottir.

# ADVOCATE Trial

- Randomized, controlled, **phase 3** trial comparing avacopan (C5a inhibitor) to a prednisone taper regimen
- Several benefits for patients with ANCA vasculitis
  - **Avacopan was superior to prednisone in sustaining remission at 52 weeks**
  - Reduced risk of serious infection vs steroid taper
    - Pneumonia
    - Granulomatosis with polyangiitis
    - Acute kidney injury
    - Urinary tract infection
  - Improved patient quality of life
  - Improved recovery of kidney function compared to glucocorticoids
  - Reduced long-term risk of end-stage renal disease

Jayne DRW, et al. *N Engl J Med.* 2021;384(7):599-609.

## Clinical Remission at Week 26

Estimated common difference, 3.4 percentage points  
95% CI, -6.0 to 12.8  
 $P < 0.001$  for noninferiority;  $P = 0.24$  for superiority

