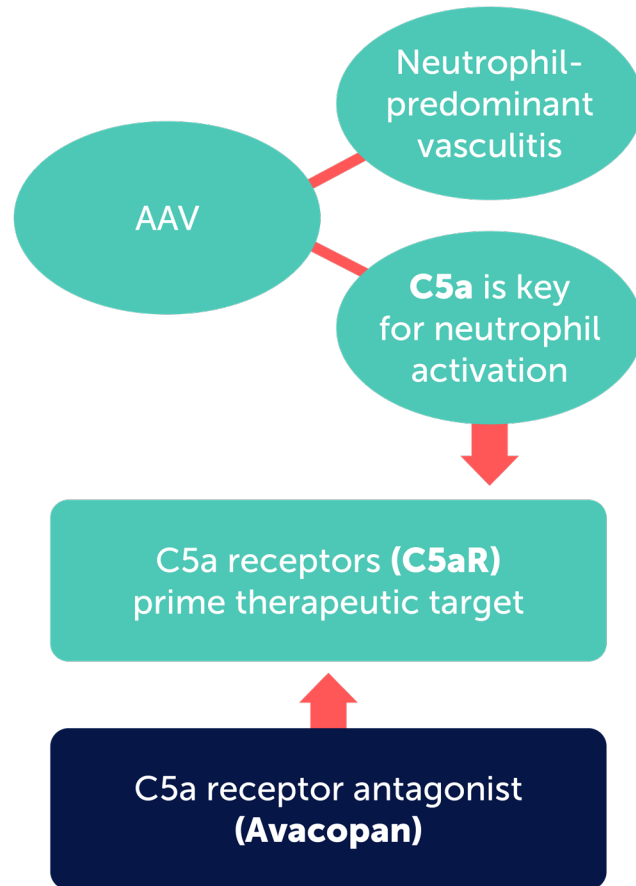


Pathophysiology of AAV



Al-Hussain T, et al. *Adv Anat Pathol.* 2017;24(4):226-234.



C5a Inhibition

C5a activates neutrophils



Release of neutrophil NETs



Split C5 & C3



↑C5a → ↑ Neutrophil attraction & activation

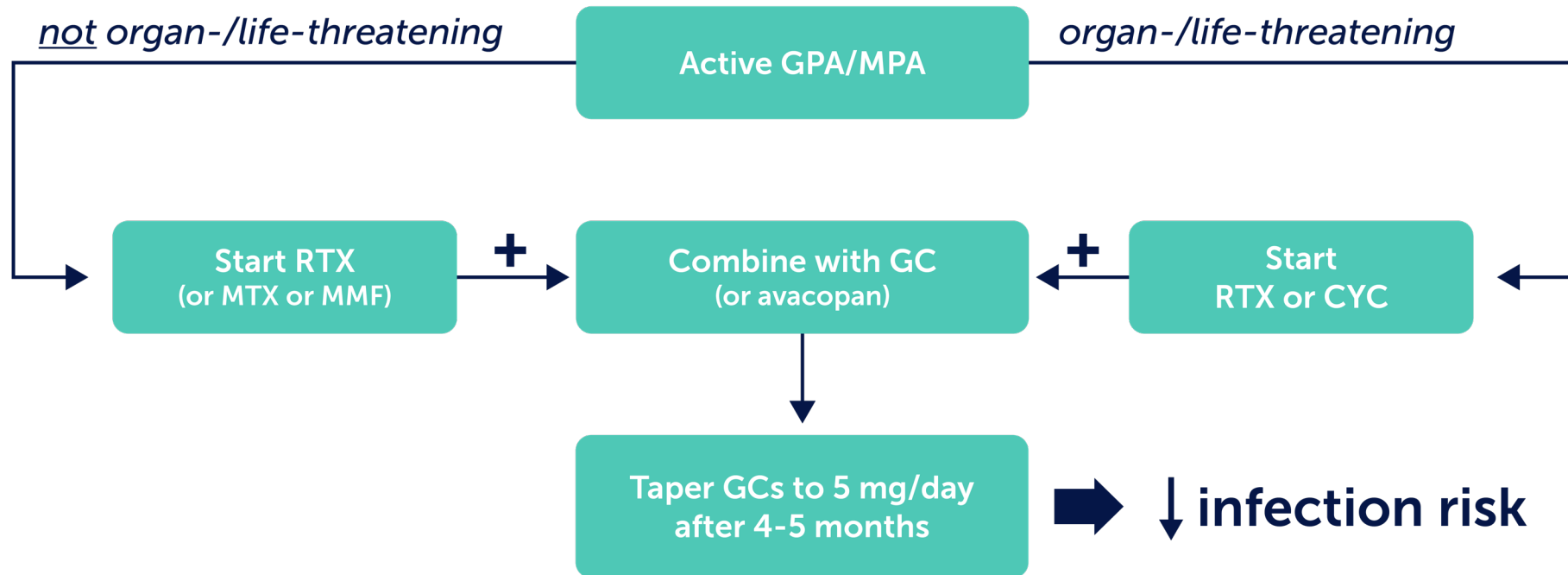


Maintained inflammatory response



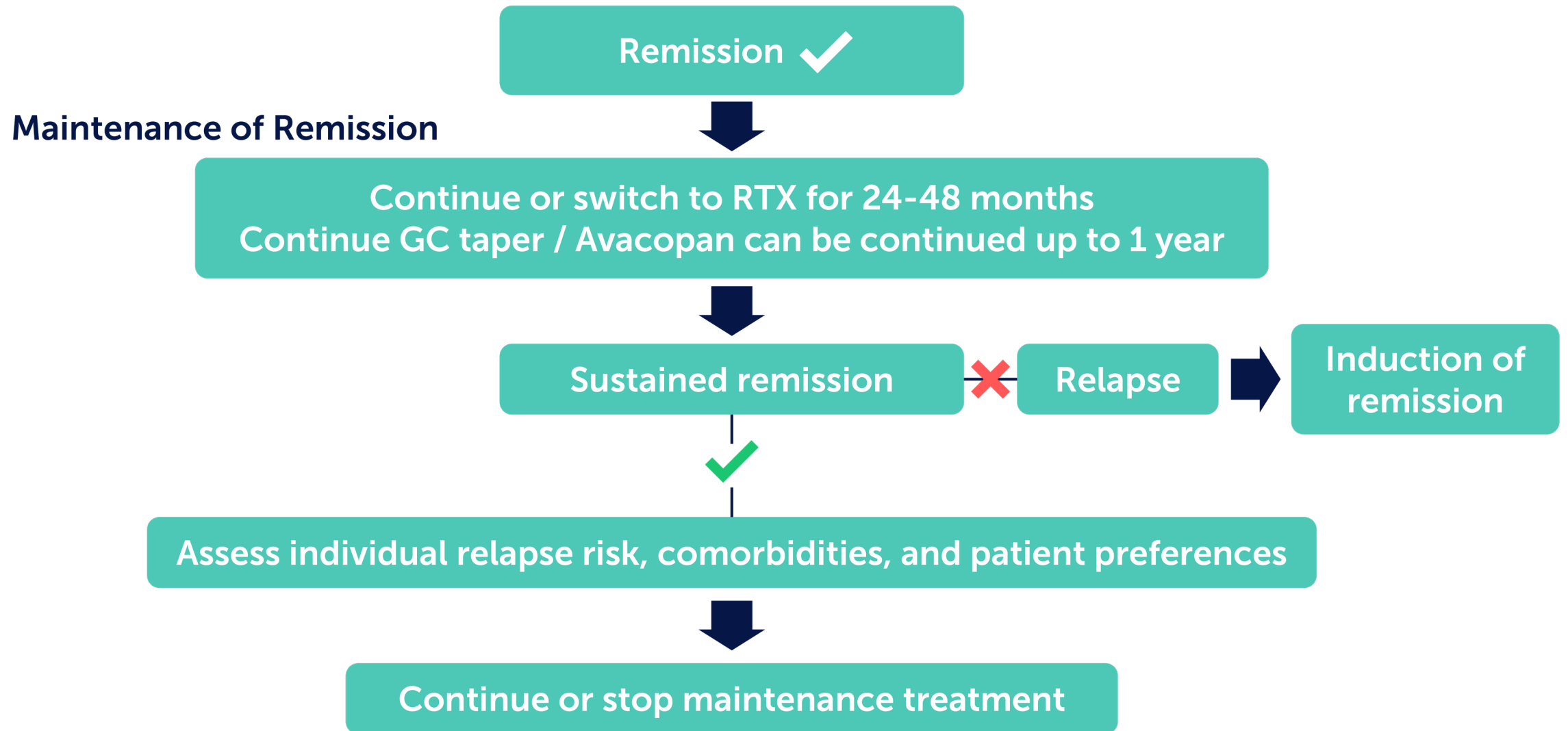
Guidelines for Managing AAV: EULAR 2022 Update

Induction of Remission



Avacopan (C5aR inhibitor) 30 mg twice daily orally + RTX or CYC may be considered for induction of remission to substantially reduce exposure to GCs.

Guidelines for Managing AAV: EULAR 2022 Update



AAV, ANCA-associated vasculitis; GC, glucocorticoid; RTX, rituximab.

Hellmich B, et al. *Ann Rheum Dis*. Published online March 16, 2023. doi:10.1136/ard-2022-223764

Turgeon D, et al. *Rheumatology (Oxford)*. 2023;62(8):2646-2651.

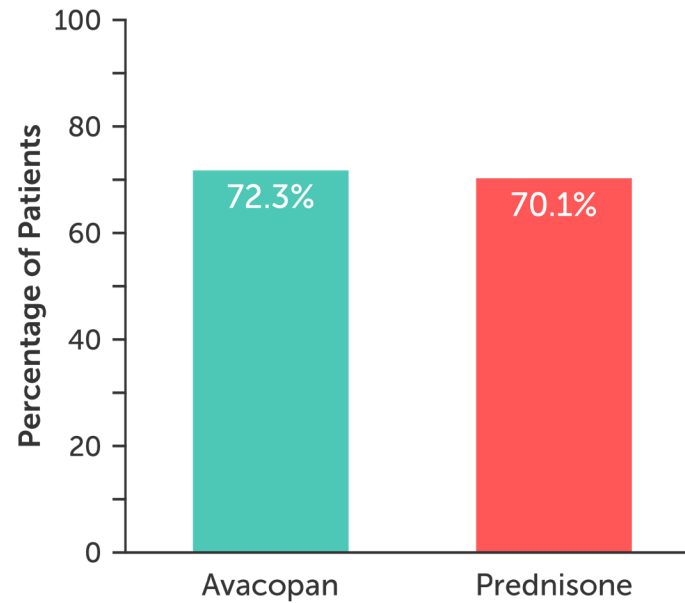
ADVOCATE Phase 3 RCT

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



Avacopan was noninferior to prednisone with respect to remission at week 26

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



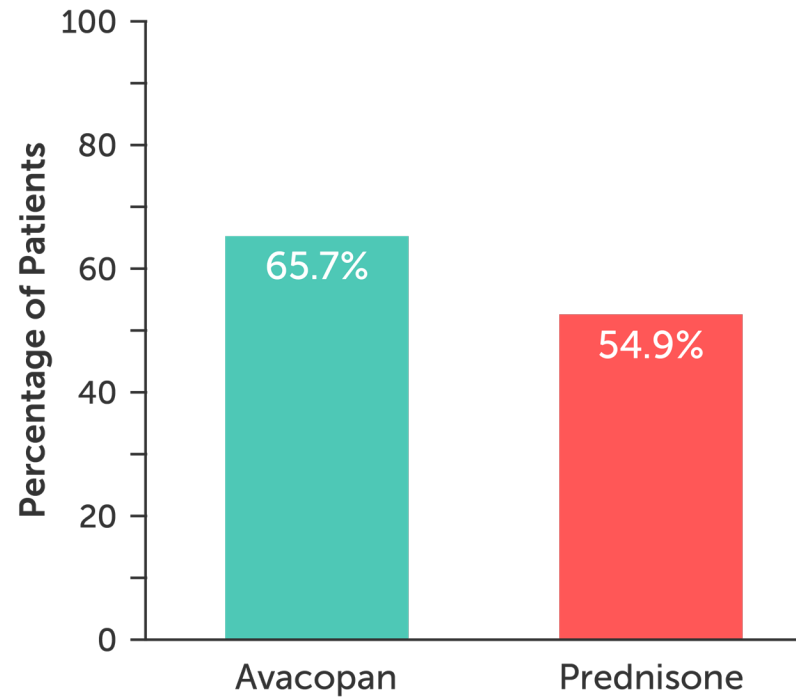
ADVOCATE: Phase 3 RCT

Clinical Remission at Week 52

Estimated common difference, 12.5 percentage points

95% CI, 2.6 to 22.3

$P < 0.001$ for noninferiority; $P = 0.007$ for superiority

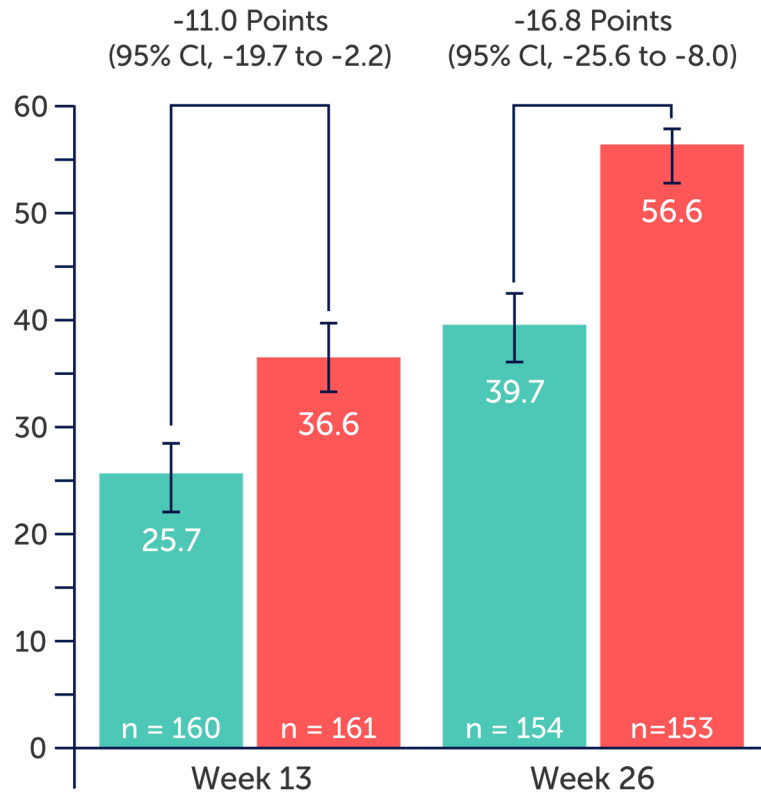


Avacopan was superior to prednisone with respect to sustained remission at week 52

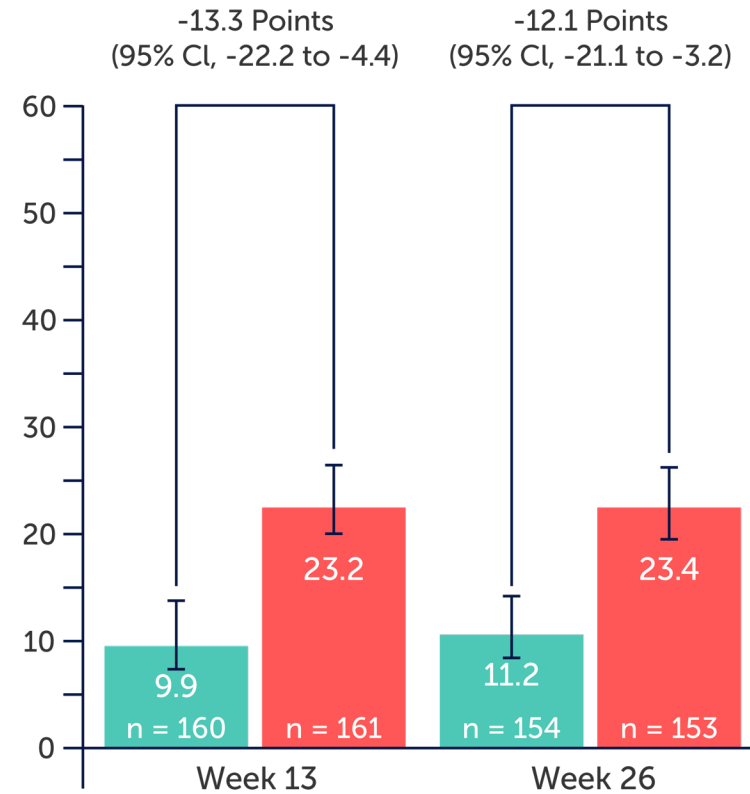


ADVOCATE: Glucocorticoid Toxicity Index (GTI)

GTI Cumulative Worsening Score (LSM)
Captures cumulative toxicity over time.
Score can only increase or stay the same.



GTI Aggregate Improvement Score (LSM)
Captures both worsening and improvement
in toxicity. Score can increase or decrease.



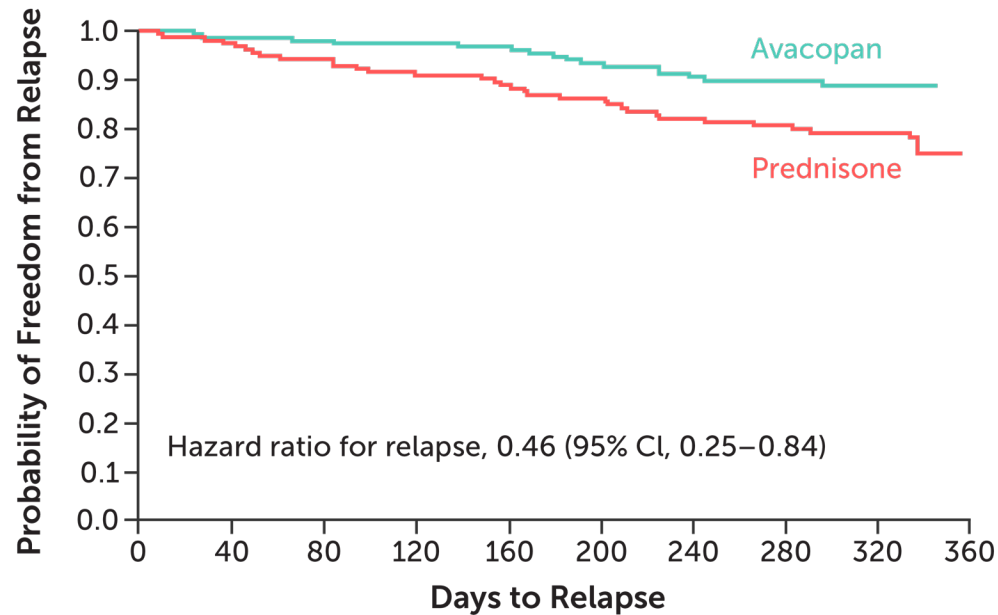
■ Avacopan ■ Prednisone

LSM, least squares mean.

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



ADVOCATE Trial



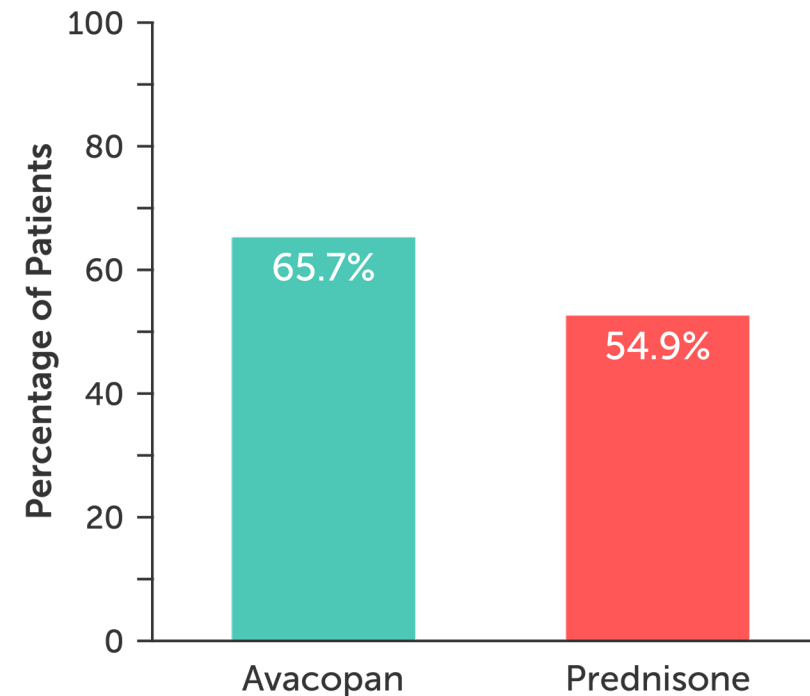
No. at Risk	0	40	80	120	160	200	240	280	320	360
Avacopan	158	153	149	146	145	133	129	115	92	0
Prednisone	157	151	146	137	133	126	119	111	90	0

10.1% of patients using avacopan experienced relapse, compared with 21% of patients treated with prednisone

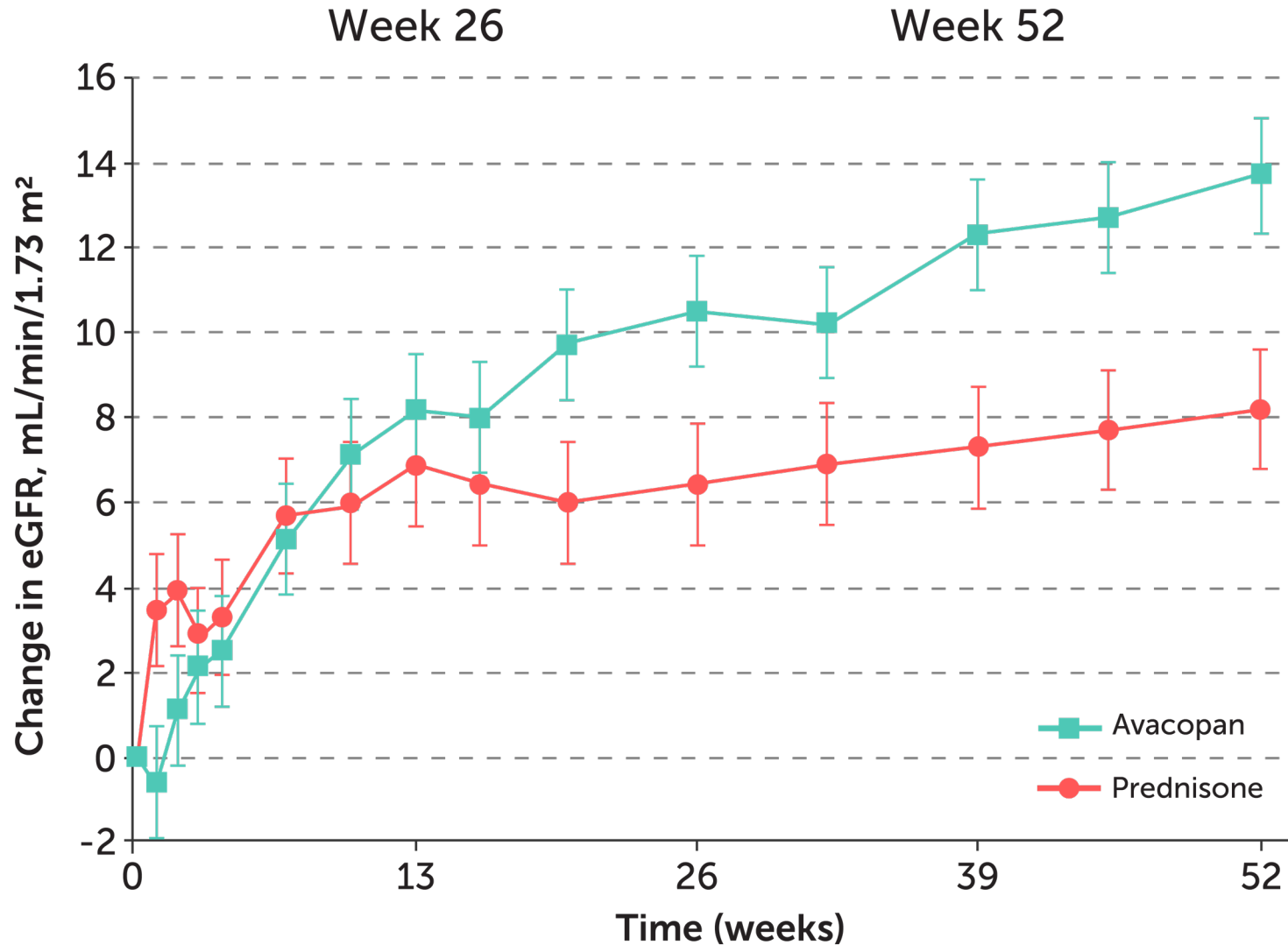
Clinical Remission at Week 52

Estimated common difference, 12.5 percentage points
95% CI, 2.6 to 22.3

$P < 0.001$ for noninferiority; $P = 0.007$ for superiority



ADVOCATE: Change in eGFR



Avacopan (C5a Inhibitor) vs Prednisone

	Avacopan
Efficacy in terms of sustained remission	↑
Safety benefit	↑
Kidney improvement	↑
Quality of life improvement	↑



Glucocorticoid Adverse Effects

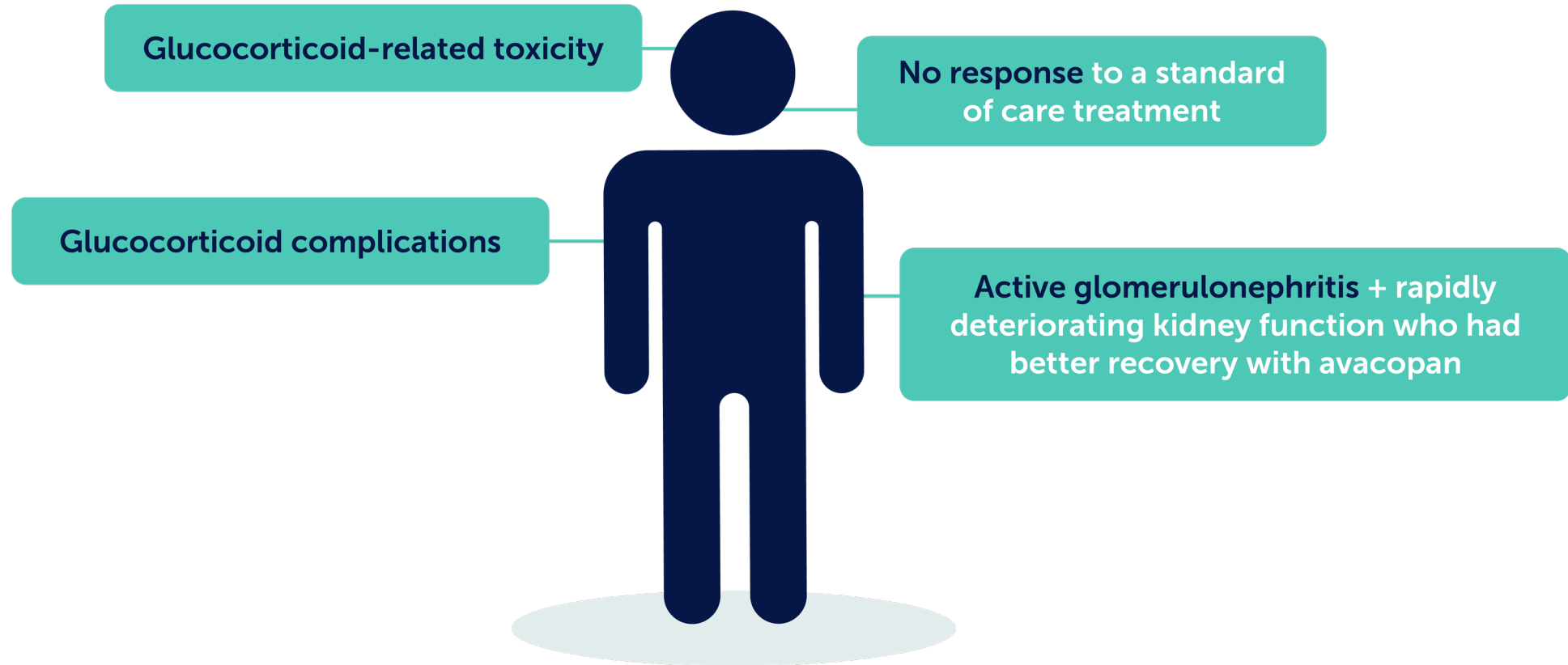
- Assess your patients for disease activity and comorbidities

Complications of Glucocorticoids
Long-term
Infections
Osteoporosis → fractures
Skin abnormalities
Hormonal abnormalities
Acute
Infections
Worsening of existing diabetes



Right Therapy for the Right Patient

- Avacopan as an alternative to glucocorticoids:
 - Combined with another agent, such as RTX



Quote by David Jayne, MD

*“...patients who are particularly likely to benefit from a C5a receptor inhibitor such as **avacopan**, namely those [at] **high risk of steroid toxicity**, those with **low GFR**, and those with **refractory disease**...”*

*“...I think **avacopan** can be considered...for **all patients** as a component of **induction therapy**.”*

