Which Oral Anticoagulant Is Best in CKD?

For patients with early CKD, non–vitamin K oral anticoagulants (NOACs) have a better risk-to-benefit profile than vitamin K antagonists (VKAs), concludes a meta-analysis in *Annals of Internal Medicine*.

In a systematic review of the literature, the researchers identified 45 randomized controlled trials that evaluated the two types of oral anticoagulants for any indication and included data on efficacy or bleeding outcomes. The studies included a total of 34,082 patients with early-stage or advanced CKD or with ESKD.

The most frequent indications were atrial fibrillation (AF) and venous thromboembolism (VTE), 11 trials each. Other indications included cardiovascular disease other than AF, 9 trials; prevention of thrombosis in dialysis access, 8 trials; and thromboprophylaxis, 6 trials. Except for 8 trials enrolling ESKD patients, the studies excluded patients with creatinine clearance less than 20 mL/min or estimated GFR less than 15 mL/min per 1.73 m^2. Most of the data came from subgroups of large trials; there was sparse evidence about patients with advanced CKD or ESKD.

On meta-analysis, NOACs were associated with a reduced risk of stroke or systemic embolism in patients with AF, compared with VKAs: risk ratio (RR) 0.79, based on high-quality evidence. Non–vitamin K oral anticoagulants were also associated with a lower risk of hemorrhagic stroke: RR 0.48, based on moderate-quality evidence.

There was no clear difference between the two types of oral anticoagulants for prevention of recurrent VTE or VTE-related mortality. Across all trials, major bleeding risk appeared lower with NOACs: RR 0.75, based on low-quality evidence.

CKD is a prothrombotic state, associated with several indications for oral anticoagulants. However, there are limited data to guide clinical decisions regarding anticoagulant therapy in CKD.

Available evidence suggests that NOACs are preferable to VKAs for patients with early CKD. The review finds scant evidence to determine the benefits or harms of these oral anticoagulants for patients with advanced CKD or ESKD. The authors emphasize the need for further adequately powered randomized trials [Ha JT, et al. Benefits and harms of oral anticoagulant therapy in chronic kidney disease: A systematic review and meta-analysis. *Ann Intern Med* 2019; 171:181–189].

Veverimer Is Effective for Metabolic Acidosis in CKD

The selective hydrochloric acid binder veverimer is a safe and efficacious treatment for metabolic acidosis in patients with CKD, according to a randomized trial report in the *Lancet*.

The study was a 40-week extension of a previous international industry-sponsored trial comparing veverimer with placebo for patients with CKD (estimated GFR 20–40 mL/min per 1.73 m^2) and metabolic acidosis (serum bicarbonate 10–20 mmol/L). In that study (*Lancet* 2019; 393:1417–1427), 59% of patients in the veverimer group met a composite primary endpoint of increased sodium bicarbonate, compared with 22% of the placebo group.

In the extension phase, 196 patients who completed the parent trial continued to receive their assigned blinded treatment for 40 weeks. Safety was the primary outcome; secondary outcomes addressed the long-term effects of veverimer on serum bicarbonate level and physical functioning.

During the extension, the premature treatment discontinuation rate was 3% in the veverimer group, in no case because of an adverse event, compared with 10% in the placebo group. The rates of serious adverse events were 2% and 5%, respectively. Veverimer was also associated with a lower

rate of renal system adverse events: 8% versus 15%.

At 52 weeks, sodium bicarbonate had normalized or increased by at least 4 mmol/L in 63% of patients assigned to veverimer, compared with 38% of the placebo group. At all times, bicarbonate concentrations were higher in the veverimer group. Veverimer was also associated with a relative 12-point improvement in the Kidney Disease and Quality of Life–Physical Function Domain and also with a 3-second difference in mean time to perform the repeat chair stand test.

Metabolic acidosis is a common and serious complication of CKD, for which there are limited approved therapies. Veverimer is an oral nonabsorbed polymer that selectively binds and eliminates hydrochloric acid from the gastrointestinal tract.

This extension study, including an analysis of 52-week outcomes, supports the safety and efficacy of veverimer in correcting metabolic acidosis in patients with CKD. In addition to lasting increases in sodium bicarbonate, this treatment produces lasting improvements in measures of physical functioning. Further studies are needed to evaluate the effects of veverimer on CKD progression and mortality [Wesson DE, et al. Long-term safety and efficacy of veverimer in patients with metabolic acidosis in chronic kidney disease: A multicentre, randomised, blinded, placebo-controlled, 40-week extension. *Lancet* 2019; 394:396–406]. ■