Cardiology guidance supports use of SGLT-2 inhibitors, GLP-1 receptor agonists for CV benefits in diabetes

ACP Diabetes Monthly Staff

A new expert consensus decision pathway calls on cardiologists to prescribe sodium-glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists to reduce cardiovascular (CV) disease risk in patients with type 2 diabetes.

"Data proving that [sodium-glucose cotransporter-2] inhibitors and [GLP-1 receptor agonists] improve outcomes in patients with [type 2 diabetes] and CV disease have triggered a major paradigm shift beyond glucose control to a broader strategy of comprehensive CV risk reduction," the authors wrote. "The potential of these compounds has also stimulated re-examination of the traditional roles of various medical specialties in the management of [type 2 diabetes], compelling CV specialists to adopt a more active role in prescribing drugs that may previously have been seen primarily as glucose-lowering therapies." This report of the American College of Cardiology Solution Set Oversight Committee was published Aug. 5 by the *Journal of the American College of Cardiology*.

Large, randomized controlled trials in patients with diabetes have demonstrated that SGLT-2 inhibitors reduce CV events in patients with atherosclerotic CV disease and/or diabetic kidney disease and reduce the risk of heart failure hospitalization, the pathway said. An SGLT-2 inhibitor is recommended for patients with diabetes and heart failure, especially heart failure with reduced ejection fraction, as well as those at high risk for heart failure, diabetic kidney disease, or CV disease. A new diagnosis of diabetes in a patient with any of these conditions should prompt a patient-clinician discussion about starting an SGLT-2 inhibitor, the pathway said.

Canagliflozin, dapagliflozin, and empagliflozin have differing FDA-approved CV indications but broadly similar CV and renal benefits, the authors wrote. Because there is no evidence of a graded dose response, physicians should start SGLT-2 inhibitors at the lowest dose tested in CV outcomes trials (100 mg for canagliflozin, 10 mg for dapagliflozin, and 10 mg for empagliflozin). No further dose titration is needed for CV or renal benefit, although doses may be increased by the clinician managing the patient's glycemic control.

A GLP-1 receptor agonist with demonstrated CV benefit is recommended for patients who have or are at very high risk for atherosclerotic CV disease. Dulaglutide, liraglutide, and injectable semaglutide have been shown to reduce major CV events, the pathway noted. Exenatide once weekly and oral semaglutide showed favorable but not statistically significant CV benefits compared to placebo. Lixisenatide did not lower risk for CV events after an acute coronary syndrome compared with placebo. GLP-1 receptor agonists should be started at the lowest dose and up-titrated stepwise to the maximum tolerated dose, the pathway recommended.

The pathway noted risks with both drug classes, including genital mycotic infections, urinary tract infections, euglycemic diabetic ketoacidosis, lower limb ulcerations, and potential volume depletion with SGLT-2 inhibitors and nausea and vomiting with GLP-1 receptor agonists. The pathway recommended using clinical judgment when starting an SGLT-2 inhibitor in patients with impaired renal function who are starting or up-titrating an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker. Caution is also suggested if patients have a history of peripheral artery disease, severe peripheral neuropathy, lower-extremity diabetic ulcers, or soft-tissue infections.

A detailed patient-clinician risk discussion is recommended before starting either drug class to review risks, benefits, and treatment options. Physicians should discuss cost because both drug classes can be expensive and out-of-pocket costs could be considerable for many patients. Differences in the route of administration between the drug classes may also influence patient and clinician decision making, the pathway said.