Study provides additional support for use of new class of diabetes drugs

24 September 2020

Credit: CC0 Public Domain

A new study led by a cardiologist from Brigham and Women's Hospital has assessed the cardiovascular and renal outcomes for ertugliflozin, an SGLT2 inhibitor prescribed for patients with type 2 diabetes to help them control blood sugar levels. The Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes Trial (VERTIS CV) found that the drug had a safety profile similar to that of other SGLT2 inhibitors and did not increase risk of major adverse events compared to the placebo. The results did not show a statistically significant benefit, but, taken together with other recent studies of SGLT2 inhibitors, the study results add to a growing body of evidence that supports guidelines for using this class of drugs to help prevent adverse cardiovascular outcomes. The findings of their study were published in the *New England Journal of Medicine*.

"This class of medications has turned out to be a huge win for patients with benefits beyond blood glucose control," said Christopher Cannon, MD, a cardiologist at the Brigham. "Originally, the Food and Drug Administration had requested analyses of the safety of these medications, but studies have found that rather than causing harm, SGLT2 inhibitors show beneficial effects, lowering risk of adverse cardiovascular and renal outcomes."

Type 2 diabetes can lead to heart failure hospitalization and renal disease progression, with adult type 2 diabetic patients and their clinicians often navigating cardiovascular and renal concerns while working to control blood sugar levels. Recent studies of other SGLT2 inhibitors have found that they may provide a benefit to both renal and cardiovascular health.

VERTIS-CV relied on an event-driven, noninferiority structure, which was revised in the wake of a positive trial involving another drug in the class. In light of the positive outcomes of that EMPA-REG trial, the VERTIS-CV team doubled its sample size and reduced the time left in the trial from five years to an average of three years. Of the 8,238 patients enrolled in the trial, the average age was 64.4 and average length of type 2 diabetes diagnosis was 13 years.

Previous studies have established ertugliflozin as an effective medication for controlling blood sugar levels. VERTIS-CV assessed the drug's cardiovascular safety. Among patients with type 2 diabetes and atherosclerotic cardiovascular disease, ertugliflozin was non-inferior to placebo for the composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke—an endpoint known as MACE. Overall, major adverse cardiovascular outcomes occurred in about 12 percent of patients in both the ertugliflozin and placebo groups. A combination of both cardiovascular death or hospitalization for heart failure occurred in about 8 percent and 9 percent in the ertugliflozin and placebo groups, respectively. A secondary endpoint of hospitalization for heart failure showed a 30 percent lower rate with ertugliflozin.

Ertugliflozin is the fourth drug in this class to be tested on such a large scale and demonstrate noninferiority against a placebo. The three other major SGLT2 drug trials—testing dapagliflozin, canagliflozin, and empagliflozin—produced significant benefits across different endpoints.

The American Diabetes Association guidelines established in 2019 recommend the use of SGLT2 inhibitors such as ertugliflozin in type 2 diabetes patients as an additional agent for lowering blood sugar and for lowering risk of cardiovascular and renal events in patients predisposed to these complications. Cannon describes his team's results as supportive of these guidelines.

"The guidelines, if anything, were a little bit ahead of their time and are spot on," said Cannon.

"These data reaffirm the guidelines, and now it's on us as clinicians to more completely follow the guidelines."

More information: Christopher P. Cannon et al, Cardiovascular Outcomes with Ertugliflozin in Type 2 Diabetes, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa2004967

Provided by Brigham and Women's Hospital