SGLT2 INHIBITORS AND CARDIOVASCULAR DISEASES: LESSONS, LEARNINGS AND THE FUTURE

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Abstract

Sodium-glucose transport protein 2 inhibitors (SGLT2is) originally emerged as antihyperglycemic agents that act independently of the pancreas. Three cardiovascular outcome trials, the CANVAS Program, DECLARE-TIMI 58 and EMPA-REG OUTCOME, that evaluated canagliflozin, dapagliflozin and empagliflozin respectively in cohorts with type 2 diabetes revealed consistent benefit on hospitalization for heart failure and cardiovascular mortality in the presence and absence of established atherosclerosis or a history of heart failure. Further analysis of the secondary readouts indicated that these SGLT2i also offer renal protection. Notably, however, only a small percentage of the participants in these cardiovascular outcome trials were at high renal risk. The positive association between SGLT2i use and preservation of renal function was cemented recently when CRENDENCE, a renal outcome trial was stopped early because of an overwhelming reduction in renal events, cardiovascular death and hospitalization for heart failure across a wide eGFR range (30 to 90 mL/min/1.73m^2). Multiple SGLT2i trials are ongoing, many of which are investigating the therapeutic potential of SGLT2i in individuals with heart failure or kidney failure regardless of whether they have diabetes. Very recent topline news from the DAPA-HF trial suggests that the SGLT2i are not yet done surprising us.

Keywords

SGLT2 inhibitors, clinical trials, cardiovascular disease, diabetes