

Cardiovascular outcomes and molecular targets for the cardiac effects of Sodium-Glucose Cotransporter 2 Inhibitors: A systematic review

Rosalinda Madonna¹, Filippo Biondi¹, Mattia Alberti¹, Sandra Ghelardoni¹, Letizia Mattii¹, and Alberto D'Alleva²

¹University of Pisa

²Gabriele d'Annunzio University of Chieti and Pescara Department of Sciences

March 24, 2024

Abstract

Sodium-glucose cotransporter 2 inhibitors (SGLT2i), a new class of glucose-lowering drugs traditionally used to control blood glucose levels in patients with type 2 diabetes mellitus, have been proven to reduce major adverse cardiovascular events, including cardiovascular death, in patients with heart failure irrespective of ejection fraction and independently of the hypoglycemic effect. Because of their favorable effects on the kidney and cardiovascular outcomes, their use has been expanded in all patients with any combination of diabetes mellitus type 2, chronic kidney disease and heart failure. Although mechanisms explaining the effects of these drugs on the cardiovascular system are not well understood, their effectiveness in all these conditions suggests that they act at the intersection of the metabolic, renal and cardiac axes, thus disrupting maladaptive vicious cycles while contrasting direct organ damage. In this systematic review we provide a state of the art of the randomized controlled trials investigating the effect of SGLT2i on cardiovascular outcomes in patients with chronic kidney disease and/or heart failure irrespective of ejection fraction and diabetes. We also discuss the molecular targets and signaling pathways potentially explaining the cardiac effects of these pharmacological agents, from a clinical and experimental perspective.

Hosted file

main text - final.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

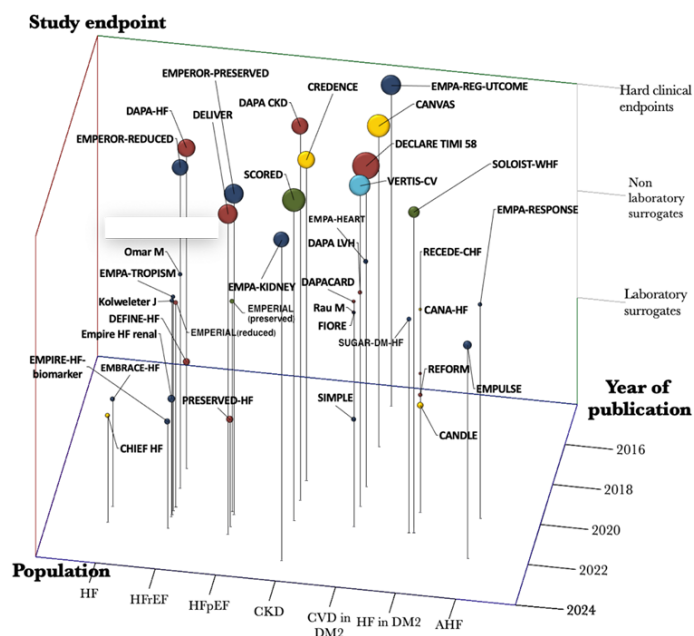


Figure 1

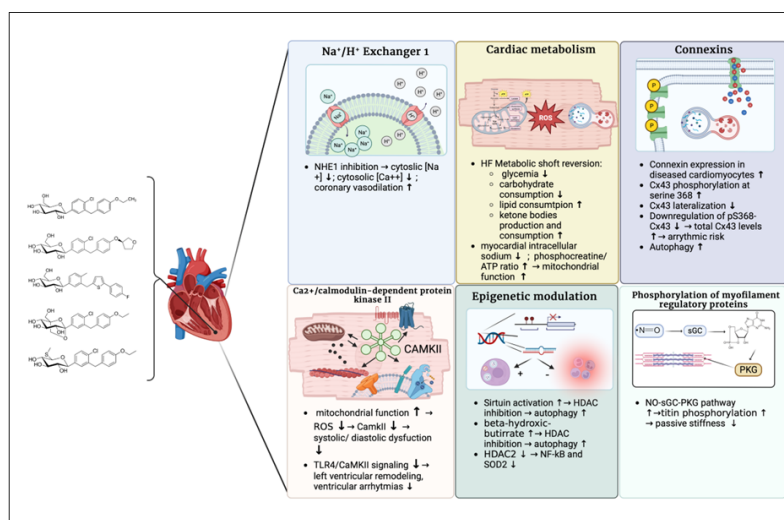


Figure 2

Hosted file

table 1 - 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

table 2- 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

table 3- 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

table 4- 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

table 5- 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

table 6- 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

table 7 - 08-02-2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

Table 8 final 02.02.2024.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>

Hosted file

Table 9 final.docx available at <https://authorea.com/users/758791/articles/733008-cardiovascular-outcomes-and-molecular-targets-for-the-cardiac-effects-of-sodium-glucose-cotransporter-2-inhibitors-a-systematic-review>