Addendum

American Diabetes Association

Addendum. 10. Cardiovascular Disease and Risk Management: *Standards of Medical Care in Diabetes—2020*. Diabetes Care 2020;43(Suppl. 1):S111–S134

https://doi.org/10.2337/dc20-ad08

Section 10, Cardiovascular Disease and Risk Management, of the *Standards of Medical Care in Diabetes—2020* has been annotated to reflect findings from the Dapagliflozin and Prevention of Adverse-Outcomes in Heart Failure (DAPA-HF) trial and the Cardiovascular Outcome Study of Linagliptin Versus Glimepiride in Type 2 Diabetes (CAROLINA).

The online version of the article (https://doi.org/10.2337/dc20-S010) reflects the changes described below.

Recommendation 10.43c (p. S123) has been revised to read:

> "In patients with type 2 diabetes and established heart failure with reduced ejection fraction, a sodium–glucose cotransporter 2 inhibitor with proven benefit in this patient population should be considered to reduce risk of worsening heart failure and cardiovascular death **A**; this may be a class effect. **C**"

The following sentence has been added to the subsection "Glucose-Lowering Therapies and Cardiovascular Outcomes" (p. S123):

> "In addition, the CAROLINA trial demonstrated noninferiority between a DPP-4 inhibitor, linagliptin, and a sulfonylurea, glimepiride, on cardiovascular outcomes despite lower rates of hypoglycemia in the linagliptin treatment group (Rosenstock, 2019)."

The following sentence has been added to the last paragraph in the subsection "SGLT2 Inhibitor Trials" (p. S126):

> "Results of the Dapagliflozin and Prevention of Adverse-Outcomes in Heart Failure (DAPA-HF) trial, which assessed the effects of dapagliflozin in patients with established heart failure (McMurray, 2019) are described in the Glucose-Lowering Therapies and Heart Failure section."

References

Rosenstock J, Kahn SE, Johansen OE, et al.; CAROLINA Investigators. Effect of linagliptin vs glimepiride on major adverse cardiovascular outcomes in patients with type 2 diabetes: the CAROLINA randomized clinical trial. JAMA. 2019;322:1155–1166. DOI: 10.1001/jama.2019.13772

McMurray JJV, Solomon SD, Inzucchi SE, et al.; DAPA-HF Trial Committees and Investigators. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019; 381:1995–2008. DOI: 10.1056/NEJMoa1911303

The last paragraph of Section 10 (p. S129) has been revised:

> The following sentences were removed—"They also suggest, but do not prove, that SGLT2 inhibitors may be beneficial in patients with established heart failure. This hypothesis is being specifically evaluated in several large outcomes trials in patients with established heart failure, both with and without diabetes, to determine the efficacy of SGLT2 inhibitors in the treatment of heart failure with reduced and preserved ejection fraction."
>
> The following sentences were added—"The EMPA-REG OUTCOME, CANVAS, DECLARE-TIMI 58, and CREDENCE trials suggested, but did not prove, that SGLT2 inhibitors would be beneficial in the treatment of patients with established heart failure. More recently, the placebo-controlled DAPA-HF trial evaluated the effects of dapagliflozin on the primary outcome of a composite of worsening heart failure or cardiovascular death in patients with New York Heart Association class II, III, or IV heart failure and an ejection

fraction of 40% or less. A total of 45% of the 4,744 trial participants had a history of type 2 diabetes. Over a median of 18.2 months, the group assigned to dapagliflozin treatment had a lower risk of the primary outcome (HR 0.74, 95% CI 0.65-0.85), lower risk of first worsening heart failure event (HR 0.70, 95% CI 0.59-0.83), and lower risk of cardiovascular death (HR 0.82, 95% CI 0.69-0.98) compared to placebo. The effect of dapagliflozin on the primary outcome was consistent regardless of the presence or absence of type 2 diabetes (McMurray, 2019). Therefore, in patients with type 2 diabetes and established heart failure with reduced ejection fraction, an SGLT2 inhibitor with proven benefit in this patient population should be considered to reduce the risk of worsening heart failure and cardiovascular death. The benefits seen in this patient population may represent a class effect. Ongoing trials are assessing the effects of several SGLT2 inhibitors in heart failure patients with both reduced and preserved ejection fraction."

Reference

McMurray JJV, Solomon SD, Inzucchi SE, et al.; DAPA-HF Trial Committees and Investigators. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019; 381:1995–2008. DOI: 10.1056/NEJMoa1911303