



Should a 'flozin be chosen to play a part for a failing heart?

Clinical Question: What is the role of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in patients with chronic heart failure with reduced ejection fraction?

Bottom Line: SGLT2i reduce mortality, heart failure hospitalizations, and improve quality of life when added to other medications in patients with heart failure with reduced ejection fraction, with or without diabetes. For every 100 patients treated with an SGLT2i for ~1.5 years, ~2 fewer will die, ~4 fewer will be hospitalized for heart failure, and ~7 will have improved quality of life (by 8 months) compared to placebo.

Evidence:

- Two industry-funded, randomized, placebo-controlled trials^{1,2} of patients with heart failure and ejection fraction $\leq 40\%$ (mainly NYHA class 2-3, 47% with diabetes, average systolic blood pressure 122 mm Hg, 65% on combination beta-blocker/renin-angiotensin system blocker/mineralocorticoid receptor antagonist³). Results statistically different unless indicated.
 - DAPA-HF:¹ 4744 patients, dapagliflozin 10mg daily.
 - At 18 months:
 - Mortality: 11.6% versus 13.9% (placebo), number needed to treat (NNT)=44.
 - Heart failure hospitalization: 9.7% versus 13.4% (placebo), NNT=27.
 - At 8 months:
 - 58.3% versus 50.9% (placebo) achieved minimal important improvement in quality of life (≥ 5 points on 100-point scale), NNT=14.
 - Adverse events: No difference.
 - EMPEROR-Reduced:² 3730 patients, empagliflozin 10mg daily. At 16 months:
 - Mortality: 13.4% versus 14.2% (placebo), not statistically different.
 - Heart failure hospitalization: 13.2% versus 18.3% (placebo), NNT=20.
 - Adverse events:
 - Genital infections: 1.7% versus 0.6% (placebo), NNH=91.
 - One meta-analysis⁴ including both trials:
 - Reduction in mortality (NNT=61) and heart failure hospitalization (NNT=24).
 - Similar efficacy in those with or without diabetes, and with or without sacubitril-valsartan.

Context:

- SGLT2i efficacy comparable to other heart failure medications:^{5,6}
 - Mortality: Relative risk reduction ~13% (others ~16-35%).
 - Heart failure hospitalization: Relative risk reduction ~30% (others ~20-35%).
- Unlike other heart failure medications, SGLT2i do not seem to cause significant hypotension or electrolyte abnormalities.^{1,2,4}
- Canadian guidelines⁷ recommend SGLT2i for patients with "mild to moderate" heart failure, though sequence not specified (e.g. whether to consider SGLT2i prior to sacubitril-valsartan).
- Splitting empagliflozin 25mg in half=12.5 mg (trial dose=10 mg) cuts cost in half (to ~\$560/year).⁸

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Disclosures:

Authors do not have any conflicts of interest to declare.

References:

1. McMurray JJV, Solomon SD, Inzucchi SE, *et al.* N Eng J Med 2019; 381:1995-2008.
2. Packer M, Anker SD, Butler J, *et al.* N Eng J Med 2020; Aug 29. doi: 10.1056/NEJMoa2022190.
3. Docherty KF, Jhund PS, Inzucchi SE, *et al.* Eur Heart J 2020; 41:2379-92.
4. Zannad F, Ferreira JP, Pocock SJ, *et al.* Lancet. 2020 Sep 19; 396(10254):819-829.
5. Lindblad AJ, Allan GM. Can Fam Physician 2014 Feb; 60:e104.
6. Sehn E, McDonald T, Lindblad AJ. Can Fam Physician 2017 Sep; 63(9):697.
7. O'Meara E, McDonald M, Chan M, *et al.* Can J Cardiol 2020; 36:159e169.
8. Alberta College of Family Physicians Price Comparison of Commonly Prescribed Pharmaceuticals in Alberta 2019. <https://acfp.ca/wp-content/uploads/2019/02/ACFPPricingDoc2019.pdf> Accessed 8 Dec, 2020.