

Should Empagliflozin and Liraglutide be Included in Cardiovascular Guidelines?

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Key Points

- Diabetes is a very strong risk factor for development of coronary heart disease and stroke – cardiovascular (CV) disease is the leading cause of morbidity and mortality in diabetic patients
- In light of safety concerns for some marketed antidiabetic therapy, the FDA released guidelines in 2008 for assessing the cardiovascular safety of new antidiabetic therapy

	Liraglutide	Empagliflozin
Mechanism	Glucagon-like peptide (GLP)-1 receptor agonist which augments glucose dependent insulin secretion, ↓ B-cell apoptosis, slows emptying	Inhibits sodium glucose cotransporter-2 (SGLT-2) which is located in the proximal tubule causing decrease in renal glucose reabsorption
Effect on CV risk factors	Reduction in weight, small reduction in SBP, increase in HR	Small reductions in weight, waist circumference, uric acid level, SBP and DBP. Small increases in LDL and HDL
Dosing	0.6 mg titrate to 1.8 mg SubQ once daily	10 mg PO once daily, may ↑ to 25 mg
Adverse effects	Nausea, vomiting, pancreatitis? (unclear)	Urinary tract infections, genitourinary fungal infections
CV trial – CV death, nonfatal MI and stroke	13% (L) v. 14.9% (P) (HR 0.87 [CI 0.78-0.97] p=0.01)	10.5% (E) v. 12.1% (P) (HR 0.86 [CI 0.74-0.99] p=0.04)
Benefits	Lower risk of hypoglycemia than sulfonylureas and insulin	
Limitations	Subcutaneous dosing only	Not studied in GFR < 30 ml/min
Place in therapy for patients w/ CV disease	Add on therapy to metformin. Also beneficial to patients on multiple agents including insulin and sulfonylureas	

SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate

- There is ongoing speculation regarding the mechanism for such immediate reduction in cardiovascular mortality with empagliflozin. The reduction in heart failure hospitalizations and mortality is intriguing and should be investigated further. Trials are underway to determine if these cardiovascular benefits will be consistent across this class of medications.
- Liraglutide has been the only agent in its class to demonstrate a reduction in cardiovascular mortality thus far. This class of medications also has a significant impact on weight reduction. Cardiovascular trials are ongoing for exenatide and dulaglutide.

References

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