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TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

Should a ‘flozin’ be chosen? Part 2: SGLT2 inhibitors in patients with chronic kidney disease

CLINICAL QUESTION

What are the effects of sodium-glucose cotransporter 2 inhibitors (SGLT2i) on patient-relevant outcomes in chronic kidney disease (CKD)?

BOTTOM LINE

For every 100 patients with CKD treated with an SGLT2i for 5 years, ~3-4 fewer will develop end-stage kidney disease (ESKD) and ~3-4 fewer will die from any cause compared to placebo. Sotagliflozin is not better than placebo for these outcomes.

EVIDENCE

- Two systematic reviews of relevant randomized, placebo-controlled trials (RCTs) included patients with CKD.[1,2] Results statistically different unless noted.
    - 52,827 patients with various cardiovascular/CKD risk. Of those with CKD, at 5 years:[1]
        - ESKD: 8.9% versus 12% (placebo), number needed to treat (NNT)=33.
        - Cardiovascular death: 11% versus 14% (placebo), NNT=27.
        - Overall mortality: 19% versus 22% (placebo), NNT=31.
    - 8 RCTs, 26,106 patients with baseline CKD, at 2.5 yrs:[2]
        - Cardiovascular disease: 10% versus 11% (placebo), NNT=91.

        - Composite kidney outcome (40-60% eGFR decline, ESKD, or renal death): 4.8% versus 6.9% (placebo), NNT=48.
    - Limitations: Included RCTs not specific to CKD patients.
- Three industry-funded RCTs[3,4,5] specific to CKD patients (neither above review included all 3 in every outcome). Mean eGFR~40-55ml/min/1.73m^2, albumin-to-creatinine ratio ~75-105mg/mmol, 67-100% had diabetes.
    - CREDENCE:[3] 4,401 patients, canagliflozin 100mg daily. At 2.6 years:
        - ESKD: 5.3% versus 7.5% (placebo), NNT=45.
        - Cardiovascular death: 5.0% versus 6.4% (placebo), NNT=71.
        - All-cause mortality: 7.6% versus 9.1% (placebo), NNT=67.
    - DAPA-CKD:[4] 4,304 patients, dapagliflozin 10mg daily. At 2.4 years:
        - ESKD: 5.1% versus 7.5% (placebo), NNT=42.
        - Cardiovascular death: 3.0% versus 3.7% (placebo), not statistically different.
        - All-cause mortality: 4.7% versus 6.8% (placebo), NNT=48.
    - SCORED:[5] 10,584 patients, sotagliflozin 200-400mg daily. At 1.3 years:
        - No difference in composite kidney outcome, cardiovascular death, or all-cause mortality.
    - Adverse events:[3-5]
        - Increase in genital infections [number needed to harm (NNH) 59-67], volume depletion (NNH=59-77), and DKA (NNH=220 to not statistically significant).
- One meta-analysis of DAPA-CKD and CREDENCE only. At ~2.5 years:[6]
    - ESKD: 5.2% versus 7.5% (placebo).
    - Cardiovascular death: 4% versus 5% (placebo).

CONTEXT

- EMPA-KIDNEY trial stopped early for benefit.[7,8]
- Guidelines[9] recommend metformin and SGLT2i first-line for patients with type-2 diabetes and CKD.
- Cost: ~$90/month.[10]

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Authors do not have any conflicts of interest to declare.

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