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COMPARATIVE EFFECTIVENESS OF SGLT2I VERSUS DPP4I ON CARDIOVASCULAR AND RENAL OUTCOMES IN ROUTINE-CARE SETTINGS

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BACKGROUND AND AIMS: While clinical trials have demonstrated the efficacy of SGLT2 inhibitors on preventing cardiovascular and renal damage, few studies have expanded this evidence to routine-care settings.
METHOD: We compared clinical outcomes of adults who started SGLT2i or DPP4i therapy in Stockholm, Sweden, during 2013-2019. The primary outcome was a composite of cardiovascular (CV) death and hospitalization for heart failure (HF). Secondary outcomes included major adverse cardiovascular events (MACE; composite of cardiovascular death, myocardial infarction, stroke), all-cause mortality and the rate of eGFR decline (eGFR slope). Propensity score weighted Cox regression was used to balance 55 variables and estimate intention-to-treat hazard ratios with 95% confidence intervals. Differences in eGFR slope were calculated with linear mixed models.
RESULTS: We identified 7136 individuals starting SGLT2i and 13,618 starting DPP4i therapy. Median age was 64 years (37% women) and median eGFR 86 ml/min/1.73m^2. During median follow-up of 2.1 years, 211 individuals developed the primary outcome, 269 experienced MACE and 178 died. After propensity score weighting, patients starting SGLT2i therapy were at lower risk for the composite of CV death/HF hospitalization (HR 0.71; 95% CI 0.53-0.94) compared with DPP4i, and showed a

tendency towards lower MACE (0.84; 95% CI 0.67-1.04) and all-cause mortality (0.85; 95% CI 0.62-1.18). There were a median of 4 (interquartile range: 2-8) eGFR measurements during follow-up per patient to estimate their eGFR slopes. In adjusted models, new users of SGLT2i had a slower rate of kidney function decline compared with DPP4i (eGFR slope difference of 0.43 (95% CI 0.15-0.72) ml/min/1.73m^2 per year). Results for the primary outcome were consistent across 7 pre-specified subgroups, including eGFR (eGFR $\geq$60: HR 0.79 [95% CI 0.57-1.08]; eGFR $<$60: HR 0.62 [0.38-0.99], p-value for interaction 0.40).

CONCLUSION: In patients undergoing routine care, initiation of SGLT2i was associated with fewer cardiovascular outcomes and less rapid kidney function decline compared with DPP4i initiation.