Comparative Effectiveness of SGLT2 Inhibitors Versus RAAS Blockers in Slowing CKD Progression Among Patients with Diabetic Nephropathy: Insights from Real-World Data

Saurabh Pandey, Vikash Verma, Louis Brooks Jr, Marissa Seligman, Shashi Khan, Abhimanyu Roy, Abhinav Nayyar, Ankit Arora, Aditi Paul, Ruchi Singhal, Ankita Bhagat, Gargi Mahashay, Anuj Gupta, Vishan Khatavkar, Shikha Anand, Archana Arya, Prateek Kumar, Atish Musle

Objective

- Diabetic nephropathy is the most common cause of end-stage renal disease in the United States.[1] Given limited real-world comparative evidence on reno-protective therapies, this study aimed to compare real-world renal outcomes among patients with diabetic nephropathy treated with SGLT2 inhibitors versus RAAS blockers.

Methodology

Study Period & Database: This retrospective cohort study used the Optum® Market Clarity database to identify patients with incident diabetic nephropathy initiating SGLT2 inhibitors or RAAS blockers. **(Figure 1).**

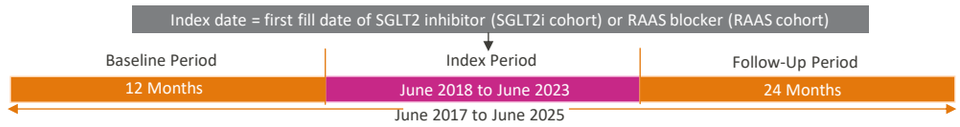

Figure 1. Study design and timeline

Cohort: SGLT2i Cohort: Patients with initial prescription fill for an SGLT2 inhibitor (Dapagliflozin, Canagliflozin, Empagliflozin, Ertugliflozin) & **RAAS Cohort:** Patients with initial prescription fill for RAAS blockers, including ACE Inhibitors (Lisinopril, Ramipril, Enalapril, Perindopril) or ARBs (Losartan, Telmisartan, Candesartan, Irbesartan, Valsartan).

Index date: First prescription fill date for drug of interest.

Inclusion criteria:

- Adult patients (≥18 years) with incident diabetic nephropathy were identified using ICD-10 diagnosis codes.
- Continuous enrollment for a 12-month baseline and a 24-month follow-up period and medication adherence (mean PDC - proportion of days covered) ≥80% for both cohorts

Exclusion criteria: Patients with ESRD or CKD stage 5, dialysis during baseline period, type 1 diabetes or gestational diabetes during the study period and patients with evidence of treatment crossover during the baseline and study follow-up period

PSM Matching: propensity score - matched (PSM) in a 1:2 ratio based on demographics (age, gender, race), Charlson Comorbidity Index (CCI), and other antidiabetic medications (Biguanides, Sulfonylureas, Alpha glucosidase inhibitors, DPP4, Insulin, GLP-1 Drugs).

Outcome: Change in estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR) after treatment initiation over a 24-month follow-up period, with CKD staging defined according to KDIGO guidelines. Improvement was defined as a transition to a less severe KDIGO stage, worsening as a transition to a more severe stage, and stability as remaining within the same stage from baseline to follow-up for both eGFR (G1–G5) and UACR (A1–A3).

Results

- A total of 13,525,664 patients with diabetic nephropathy were identified; following inclusion & exclusion criteria 21,300 and 273,979 patients were included in the SGLT2i and RAAS cohorts, respectively.
- After PSM, the final analysis included 17,364 patients in SGLT2i Cohort and 34,728 patients in RAAS Cohort.
- In the matched cohorts, most patients were aged ≥60 years (RAAS: 86.3%; SGLT2i: 81.0%), and Caucasian patients represented the largest racial/ethnic group (RAAS: 65.0%; SGLT2i: 61.2%).
- From baseline to follow-up, UACR improved, remained stable, and worsened in 15.8% vs 14.7%, 72.8% vs 71.0%, and 11.2% vs 14.1% of SGLT2 inhibitor versus RAAS blocker users, respectively, while eGFR improved, remained stable, and worsened in 14.5% vs 17.7%, 58.9% vs 56.3%, and 26.5% vs 25.9%. **(Figures 2 and 3).**
- eGFR decline (≥40%) from baseline to follow-up was more frequent in the RAAS cohort than in the SGLT2i cohort (20.5% vs 0.55%) whereas overall changes in eGFR and UACR did not differ significantly between cohorts (eGFR p=0.3754; UACR p=0.3567).
- Transition-matrix analyses demonstrated stability in kidney outcomes across cohorts from baseline to follow-up:
  - ✓ eGFR: The SGLT2i cohort showed greater stability in intermediate stages, with 62.1% remaining in G3b and 68.9% remaining in G4, compared with 52.9% (G3b) and 61.8% (G4) in the RAAS cohort. Progression from G4 to G5 was lower with SGLT2i (5.0%) than with RAAS blockers (13.8%) (OR: 2.0, 95% CI 1.4-2.8, p<0.001).
  - ✓ UACR: More favorable albuminuria patterns were observed with SGLT2i use, including higher maintenance of A1 (82.0%) and greater transitions from A2 to A1 (27.9%), compared with 77.1% and 26.2%, respectively, in the RAAS cohort, while persistence of severe albuminuria was higher with RAAS (A3: 74.2% vs 63.5%). **(Fig 1).**

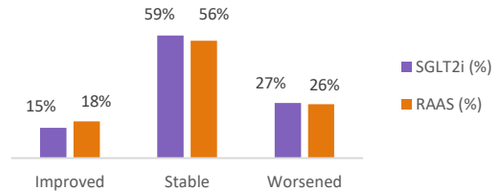

Figure 2. eGFR Outcome Categories from Baseline to Follow-up

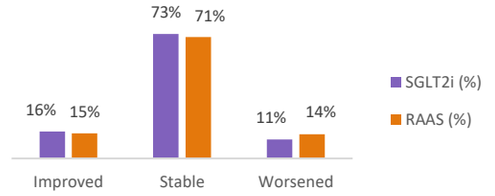

Figure 3. UACR Outcome Categories from Baseline to Follow-up

Outcome categories were defined by KDIGO stage transitions between baseline and follow-up (improved = stage decrease; stable = no change; worsened = stage increase).

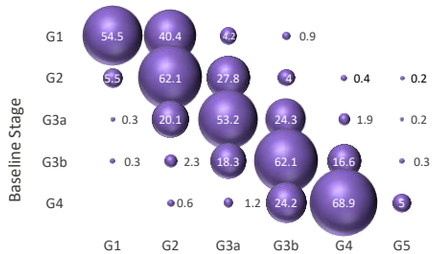

Fig 1.1. eGFR Stage Changes (SGLT2i Cohort, %)

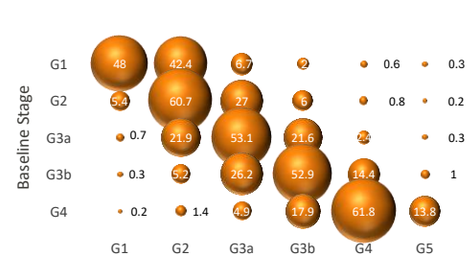

Fig 1.2. eGFR Stage Changes (RAAS Cohort, %)

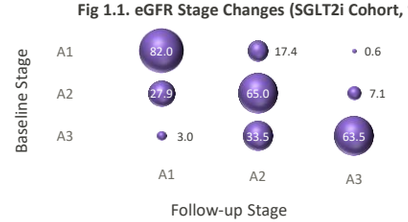

Fig 1.3. UACR Stage Changes (SGLT2i Cohort, %)

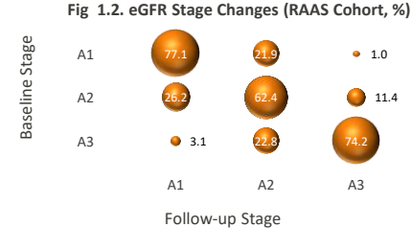

Fig 1.4. UACR Stage Changes (RAAS Cohort, %)

Fig 1. Baseline-to-follow-up changes in eGFR and UACR categories in the SGLT2i and RAAS cohorts

Conclusions

- Overall, both SGLT2 inhibitors and RAAS blockers were associated with stabilizing kidney function, SGLT2 inhibitor use showed comparatively greater renal benefit, reflected by improved eGFR stage stability, lower progression to advanced CKD, and more favorable albuminuria trajectories in real-world patients with diabetic nephropathy. Extended follow-up period is required to more comprehensively characterize the long-term reno-protective outcomes of SGLT2 inhibitors.

References: 1. Kovács GL. 6. Diabetic Nephropathy. EJIFCC. 2009 Apr 20;20(1):41-53. PMID: 27683326; PMCID: PMC4975269.
2. Hunsuwan, Supattra, et al. "Real-world effectiveness and safety of sodium-glucose co-transporter 2 inhibitors in chronic kidney disease." Scientific reports 15.1 (2025): 1667.