Observational Study Results Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Overall data disclosed, may differ from published or presented data and are a reflection of the limited information provided here. The results from a single study need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

1. Abstract

Acronym/Title	FINEGUST/**FINE**renone dru**G** **U**tilization **S**tudy and assessment of **T**emporal changes following availability of different treatment options in patients with chronic kidney disease and type 2 diabetes
Report version and date **Author**	v 1.0, 06 MAR 2025 PPD, RTI-HS PPD, RTI-HS PPD, RTI-HS PPD, Bayer AG
GEMSTONE/IMPACT study number	21956
Keywords	Chronic kidney disease; type 2 diabetes; cohort study; drug utilization patterns; pre-finerenone; post-finerenone
Rationale and background	Patients with chronic kidney disease (CKD) are at high risk of kidney failure, cardiovascular disease, and death. Patients with type 2 diabetes mellitus (T2D) have a high prevalence and incidence of CKD. Prevention, early detection, and treatment of CKD may result in improved patient outcomes, especially among patients with diabetes. Approved therapies to prevent and treat CKD among patients with T2D include angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), sodium-glucose cotransporter 2 inhibitors (SGLT2i), and glucagon-like peptide-1 receptor agonists (GLP-1 RA). Steroidal mineralocorticoid receptor antagonists (sMRA) are also used for the treatment and prevention of CKD in patients with T2D but are not approved for this indication. Finerenone is an oral, selective, non-steroidal mineralocorticoid receptor antagonist (nsMRA) developed by Bayer for the treatment of CKD in patients with T2D. Finerenone has been approved by the United States (US) Food and Drug Administration, the European Medicines Agency (EMA), and the Japanese Pharmaceutical and Medical Devices Agency (PMDA). The clinical landscape for the treatment of patients with CKD and T2D is rapidly evolving with the introduction of new treatments, and it is of interest to study how treatment patterns

	may have evolved with the approval of new drugs for this indication.
Research question and objectives	The overall aim of this study was to describe patient profiles and treatment patterns in medication initiator cohorts of patients with CKD and T2D. The primary objective was to describe baseline patient characteristics, comorbidities, and comedications in adult patients with CKD and T2D who initiate an SGLT2i, a GLP-1 RA, an sMRA, finerenone, or other nsMRA (only in Japan) in each of two time periods corresponding to finerenone pre-launch and post-launch dates. The secondary objectives were to describe: 1) treatment changes over time in the initiator cohorts, including treatment discontinuation, treatment switches, add-on treatments, and titration (finerenone only) in each of two time periods corresponding to finerenone pre-launch and post-launch dates, and 2) temporal changes in the baseline characteristics of the medication-specific cohorts before and after finerenone launch.
Study design	A multidatabase, multinational, observational (non-interventional) cohort study was conducted to describe drug utilization and temporal changes of different treatment options in adults with CKD and T2D using secondary data from data sources in the EU, Japan, and the US. The study identified separate medication-specific cohorts in two separate time periods corresponding to the pre-approval and post-approval dates of finerenone; dates of the time periods varied in each of the study countries. In the pre-finerenone period (study period I), four new-user cohorts were identified, based on the first use of any drug in these classes: SGLT2i, GLP-1 RA, sMRA, or nsMRA. The nsMRA cohort was only identified in Japan, where esaxerenone is available. In study period II (post-finerenone), new-user cohorts for SGLT2i, GLP-1 RA, and finerenone were created in a single data source (CDM) with an adequate number of finerenone users.
Setting	US, Denmark, Japan, The Netherlands, Spain
Subjects and study size, including dropouts	<u>Pre-finerenone:</u> • SGLT2i = 21,739 (DNHR); 381 (PHARMO); 31,785 (VID); 1,157 (J-CKD-DB-Ex); 56,219 (CDM) • GLP-1 RA = 18,929 (DNHR); 476 (PHARMO);

	11,798 (VID); 329 (J-CKD-DB-Ex); 70,158 (CDM) • sMRA = 12,689 (DNHR); 2,691 (PHARMO); 14,906 (VID); 1,769 (J-CKD-DB-Ex); 71,716 (CDM) • nsMRA = 63 (J-CKD-DB-Ex) <u>Post-finerenone (CDM):</u> • SGLT2i = 94,080 • GLP-1 RA = 72,816 • Finerenone = 3,591 • Wide Finerenone = 5,201 Across all cohorts, the greatest proportion of individuals were excluded from the cohort due to either having another prescription in the same medication class in the prior 12 months or not having a diagnosis of CKD.
Variables and data sources	The study was conducted in five data sources: DNHR (Denmark), PHARMO (The Netherlands), VID (Spain), J-CKD-DB-Ex (Japan), and CDM (US). Information on patient characteristics (e.g., age, sex), laboratory values (e.g., eGFR, HbA_{1c}), medication use, and diagnosis of comorbid conditions was obtained from each of the data sources for analysis.
Results	In study period I (pre-finerenone), common findings across all data sources were that ACEi or ARB medications were by far the most frequent medication types used before initiation of the index GLP-1 RA or SGLT2i, and hypertension was the most frequently recorded medical comorbidity. Most patients had used glucose-lowering drugs (GLD) in the 180 days before or on the index date, but the type of GLD used varied by data source, with metformin being the most frequently used GLD before SGLT2i or GLP-1 RA initiation in the data sources in Denmark, The Netherlands, and the US and dipeptidyl peptidase-4 inhibitors (DPP-4i) in the data sources in Japan and Spain (for SGLT2i only). For the SGLT2i cohort, treatment patterns during follow-up and the proportion of patients observed to be receiving treatment at each timepoint were similar among the DNHR, VID, and J-CKD-DB-Ex data sources. The largest proportional increase in the "no exposure" treatment state occurred between the 90-day and 180-day timepoints in each data source except for PHARMO, in which the proportion of patients not treated increased the most between two and three years. Within the GLP-1 cohort, the largest proportional increase in the "no exposure" treatment state occurred within the first six months of initiation (between

	the index date and the 90-day timepoint or between the 90-day timepoint and the 180-day timepoint). Patients within the sMRA cohort were notably different than the other medication cohorts. Initiators were older, with less severe T2D but with more complications, more advanced CKD, and a higher prevalence of heart failure as a comorbid condition. In study period II (post-finerenone), treatment intensity for T2D was more pronounced in the finerenone cohorts than in the other two cohorts (GLP-1 RA and SGLT2i) as reflected by more use of T2D medications (including insulin). Conversely, metabolic control as measured by HbA1c levels was better in the finerenone cohorts. A higher percentage of patients were in CKD stages 3 and 4 in the finerenone cohorts than in the other two cohorts of interest (GLP-1 RA and SGLT2i). In CDM (the only data source used to assess trends in the post-finerenone period), 18.0% of patients received the 20-mg dose of finerenone at baseline, and the rest received the 10-mg dose. Among patients receiving the 10-mg dose of finerenone at baseline, approximately 17% of patients had been titrated up to 20 mg at 12 months after cohort entry. Regarding concomitant medications, use of ARB, statins, and calcium channel blockers was more common in the finerenone cohorts than in the other two cohorts (GLP-1 RA and SGLT2i in the post-finerenone period). For both the GLP-1 RA and SGLT2i medication cohorts, patients in the post-finerenone period had lower severity of T2D but greater severity of CKD compared with the pre-finerenone period. In the SGLT2i cohort, the comorbidity burden was greater in the post-finerenone period (compared with the pre-finerenone period), but this trend was not observed in the GLP-1 RA cohort.
Discussion	In this study population with CKD and T2D in 2012-2021, largely before the approval of new CKD indications for existing treatments (SGLT2i and GLP-1 RA) and new CKD treatments (e.g., finerenone), treatment options and therapeutic approaches were heterogeneous and dynamic both within and among data sources. At one year of follow-up, half or more of patients who initiated an SGLT2i were currently receiving SGLT2i treatment across the data sources. We observed a steady increase in GLP-1 RA use across data sources during the study period, and persistence with treatment was high. Findings suggest that GLP-1 RA use is related to

	both severity of T2D and the presence of obesity. The sMRA cohort had a different clinical profile than the other two cohorts, which may be related to the fact that sMRAs are not indicated to treat T2D but may be used to treat resistant hypertension and heart failure, which are common among patients with T2D. In CDM, the differences observed between the pre- and post-finerenone periods in the SGLT2i and GLP-1 RA cohorts are likely related to changes in clinical guidelines that mainly involved SGLT2i medications. The percentage of patients receiving a 20-mg finerenone dose at cohort entry was consistent with the percentage of patients with eGFR levels at baseline that are recommended for this dosage. However, up-titration to the 20-mg daily dose among patients initially taking the 10-mg dose occurred in a lower percentage of patients than expected. The treatment landscape for the prevention of CKD progression in patients with T2D is evolving rapidly. Understanding the characteristics and patterns of use of existing treatments and characterizing the differences in populations and treatment patterns across data sources is a first step in designing future studies to evaluate kidney and cardiovascular outcomes with treatment to prevent CKD progression.
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