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Practical News, Trends, and Analysis

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PRESSURE DROPS, RISKS RISE

Study Finds As-Needed BP Medications Increase AKI Risk

PLUS....

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Contents

June 2025
VOLUME 17, NUMBER 4

Conference Coverage

Boston, Massachusetts | April 10-13, 2025

NATIONAL KIDNEY FOUNDATION SPRING CLINICAL MEETINGS 2025

Nephrologists, fellows, and residents with a special interest in kidney disease, general internists, pharmacists, physician assistants, nurse practitioners and nurses, technicians, social workers, and renal and clinical dietitians all attended the 2025 National Kidney Foundation Spring Clinical Meetings (SCM25) in Boston, Massachusetts, to learn about developments in all areas of nephrology practice and network with colleagues. Presenters reported the latest insights into chronic kidney disease care, and participants were informed about new and evolving concepts related to kidney disease.

Blood Volume Monitoring Improves Outcomes for Patients Hospitalized With HF

Patients receiving hemodialysis commonly require hospitalization and rehospitalization for heart failure (HF), due, in part, to difficulties associated with accurate assessment of volume as well as incorrect ultrafiltration targets.

Researchers conducted a retrospective study to examine a possible association between incorporating blood volume monitoring (BVM) for patients receiving hemodialysis and hospitalized with HF to inform decisions regarding ultrafiltration and improved clinical outcomes. The researchers reported results of the study at SCM25.

The study was conducted at two hospitals in Boston, Massachusetts; one used BVM routinely and the other did not. Before the availability of BVM, the outcomes at the two hospitals were similar. Eligible patients were adults receiving maintenance hemodialysis admitted with exacerbations of HF. The primary outcome of interest was length of index hospitalization. Secondary outcomes were time to decongestion, rates of rehospitalization for HF at 90 and 180 days after initial discharge, and time to rehospitalization for HF. Outcomes were extracted from electronic health records and adjudicated by two nephrologists.

The cohort included 278 patients. Mean age was 70 years, 58% were male, and 62% were White. The average length of the index hospitalization was 7 days. After adjustment for baseline characteristics, there was an association between BVM and a shorter length of stay (difference of -2.00 days; 95% CI, -4.20 to -0.30), faster time to decongestion, and lower rates of rehospitalization at both 90 days and 180 days after index discharge.

In conclusion, the authors said, "Incorporating BVM in managing hemodialysis patients with HF was associated with improved clinical outcomes, including shorter length of stay, faster decongestion, and reduced hospitalization rates. These findings support the need for prospective studies to optimize volume management and improve outcomes in this challenging patient population."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-295. doi:10.1053/j.ajkd.2025.02.296

Prevalence of CKM Among US Adults Increased Over Time

Cardiovascular-kidney-metabolic (CKM) syndrome has been defined by a recent presidential advisor from the American Heart Association as "an adverse and progressive interplay of obesity and key metabolic alterations, chronic kidney disease (CKD), and cardiovascular diseases (CVD)."

Researchers at the University of Michigan, Ann Arbor, performed an analysis of 2001-2020 data from the National Health and Nutrition Examination Survey to assess the burden of CKM syndrome on the US population over time to help inform its prevention and management. Results were reported during SCM25.

Adults aged 18 years and older were categorized into five CKM stages as follows: (1) stage 0, no CKM risk factors; (2) stage 1, excess or dysfunctional adiposity (overweight/obesity, abdominal obesity); (3) stage 2, metabolic risk factors and CKD (hypertension, hypertriglyceridemia, diabetes/prediabetes, metabolic syndrome, Kidney Disease: Improving Global Outcomes [KDIGO] moderate-to-high risk CKD); (4) stage 3, subclinical CVD in CKM (KDIGO very high risk CKD, high predicted risk CVD); and (5) stage 4, clinical CVD in CKM. Weighted logistic regression was used to examine the population burden of CKM and its stages over time.

Overall prevalence of CKM increased from 76.5% in 2001-2004 to 82.2% in 2017-2020; there was a corresponding decline in CKM stage 1. Stage 1 CKM had the largest increase over time, with 6% higher odds or 9% age-adjusted higher odds ($P<0.001$) per 4-year cohort. The decline in the prevalence of stage 0 CKM was observed in all race and ethnic groups; it was highest among Hispanic adults.

In summary, the researchers said, "CKM syndrome in US adults has increased over the past 20 years, with a significant decline in the proportion of people with no CKM risk factors (ie, CKM stage 0). In particular, the rising prevalence of stage 1 CKM may be an opportunity for earlier detection and management of obesity and screening for components of CKM (including CKD) to potentially prevent progression to more advanced stages of CKD, including CKD and cardiovascular disease."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-300. doi:10.1053/j.ajkd.2025.02.301

Baseline Characteristics in VISIONARY Trial of Sibeprenlimab

The phase 2 ENVISION study of sibeprenlimab revealed that the investigational drug significantly reduced proteinuria and stabilized estimated glomerular filtration rate (eGFR) among patients with immunoglobulin A nephropathy (IgAN). Sibeprenlimab is a humanized IgG2 monoclonal antibody that blocks the action of the B-cell growth factor APRIL (a proliferation-inducing ligand).

At SCM25, researchers presented baseline characteristics of patients in the phase 3 VISIONARY (NCT05248646) trial. VISIONARY, the largest phase 3 trial of an IgAN treatment to date, is intended to evaluate the efficacy and safety of sibeprenlimab.

The ongoing, multicenter, double-blind, placebo-controlled study enrolled 510 patients from five continents who had IgAN and were at high risk for disease progression. Participants' median age was 42 years, 58.8% were male, 59.0% were Asian, 36.7% were White, 0.8% were Black, and 3.5% were identified as "other" race. The mean (SD) systolic BP was 123.7 (11.7) mm Hg and mean (SD) diastolic BP was 78.5 (8.5) mm Hg.

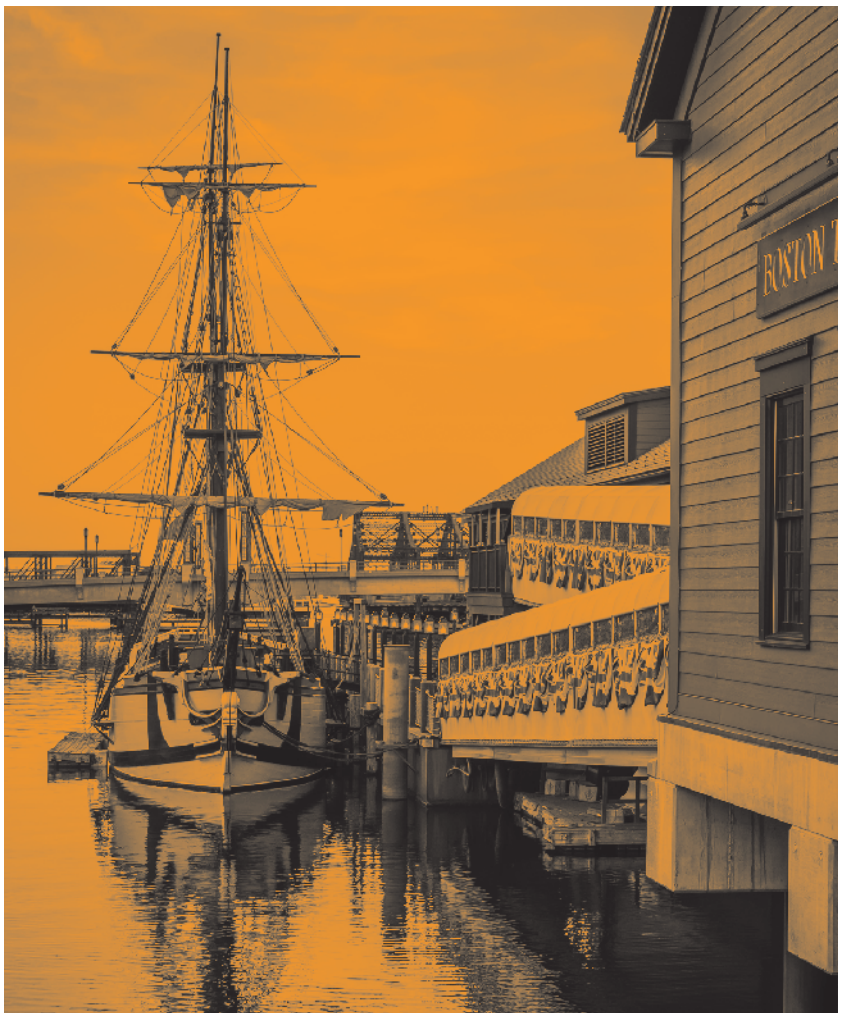
The mean (SD) 24-hour urine protein to creatinine ratio (UPCR) was 1.5 (0.9) g/g, and median 24-hour UPCR was 1.3 g/g. Of the total cohort, 402 (78.8%) patients had a screening 24-hour UPCR of 2.0 g/g or less, and 108 (21.2%) had a screening UPCR greater than 2.0 g/g. The mean (SD) 24-hour urine protein excretion was 2.1 (1.3) g/24 h. The median eGFR was 60.0 mL/min/1.73 m^2. Nearly all patients (97.8%) received renin-angiotensin system blockade therapy, and 45.1% received sodium-glucose cotransporter-2 inhibitors.

The study randomized patients with IgAN 1:1 to either receive sibeprenlimab 400 mg or subcutaneous placebo once every 4 weeks for a total of 26 doses. The primary end point is the relative change from baseline UPCR in 24-hour urine at month 9.

With a large, diverse study population, VISIONARY is expected to be broadly applicable to real-world clinical practice. Clinical results will be reported later in 2025.

Funding for the study was provided by Otsuka Pharmaceutical Development & Commercialization, Inc.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-378. doi:10.1053/j.ajkd.2025.02.379



Conference Coverage

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Conservative Management Versus Dialysis for Patients With Advanced CKD

Although the prevailing treatment paradigm for patients with advanced CKD progressing to end-stage kidney disease is dialysis, there is increasing interest in conservative management (CM). In certain subgroups of patients with advanced CKD, CM offers an alternative, patient-centered treatment strategy.

Researchers conducted an analysis among a cohort of US veterans with advanced CKD to compare the impact of CM on the risk of cognitive dysfunction with that of transition to dialysis. Results were reported at SCM25.

The analysis included linked national data from the Veterans Association, United States Renal Data System, and Medicare. Advanced CKD was defined as having two or more eGFRs of 25 mL/min/1.73 m^2 or less separated by 90 days or more. Patients with advanced CKD were identified as not receiving dialysis within 2 years of the index eGFR (CM) or receiving dialysis within 2 years of the index eGFR. Using unadjusted and doubly adjusted Cox models, the researchers compared the risk of incident dementia, mild cognitive impairment (MCI), and dementia or MCI (combined dementia/MCI) in the two groups.

A total of 90,017 patients met the eligibility criteria. Of those, 15,844 developed dementia, 3,406 developed MCI, and 16,858 developed dementia or MCI. In unadjusted models, there was an association between transition to dialysis and higher risk of incident dementia (hazard ratio [HR], 1.40; 95% CI, 1.31-1.49), MCI (HR, 1.39; 95% CI, 1.23-1.58), or combined dementia/MCI (HR, 1.26; 95% CI, 1.28-1.44) compared with CM. Results were similar in sensitivity analyses doubly adjusted for propensity score covariates.

"In a national cohort of veterans, transition to dialysis was associated with higher risk of dementia and MCI versus CM," the researchers said. "Further studies are needed to determine the mechanistic pathways underlying the differential risk of cognitive dysfunction across advanced CKD treatment strategies."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-405. doi:10.1053/j.ajkd.2025.02.406

Interim US Results From the FINE-REAL Study

At SCM25, researchers reported results of an interim analysis (cutoff, June 13, 2024) of participants in the FINE-REAL (NCT05348733) study.

FINE-REAL is a global, prospective, single-arm, noninterventional study of finerenone in clinical practice in adult participants aged 18 years and older with CKD and type 2 diabetes. The interim analysis results describe characteristics, concomitant therapy, dosing, treatment patterns, and safety of finerenone in US participants.

The US cohort included 774 participants. Mean age was 66 years, 1.9% were younger than 40 years, 54% were male, and 19.9% were Black. Median follow-up was 341 days. At baseline, median UACR was 200 mg/g (n=332), and mean eGFR was 52 mL/min/1.73 m^2.

At initiation of finerenone, use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor-neprilysin inhibitors was 71.3%; sodium-glucose transport protein 2 inhibitor (SGLT2i) use was 43.0%; and glucagon-like peptide-1 receptor agonist (GLP-1 RA) use was 32.6%. Using KDIGO risk criteria, participants were classified as being at low (1.8%), moderate (8.0%), high (11.0%), or very high (18.5%) risk.

Finerenone was initiated at 10 mg in 85.8% of participants and at 20 mg in 14.1%. In 21.8% of those initiated at 10 mg, the dose was uptitrated; in 5.5% of those initiated at 20 mg, the dose was downtitrated.

Of all participants, 33.5% experienced treatment-emergent adverse events (TEAEs). The most common TEAEs were urinary tract infection (4.0%), urogenital tract hemorrhage (3.7%), and renal failure (2.2%). There were serious TEAEs in 8.1% of participants and study drug-related TEAEs in 9.2%. Hyperkalemia was observed in 6.8% of participants. Eight events led to discontinuation of the study drug. There were no deaths.

"The FINE-REAL US cohort was at lower KDIGO risk than in finerenone phase 3 trials and more often received SGLT2i/GLP1-RA," the authors said. "Finerenone was well tolerated; safety was consistent with the known profile."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-421. doi:10.1053/j.ajkd.2025.02.422

GLP-1 RA Use and Kidney Outcomes in Young-Onset Type 2 Diabetes

Studies among patients aged 21 years and younger have shown that GLP-1RAs are associated with reductions in HbA1c and BMI. However, data on kidney outcomes in this patient population are limited.

To examine the effects of GLP-1 RAs on kidney function in adolescents and young adults with youth-onset type 2 diabetes (YO-T2D), researchers conducted a retrospective analysis of data from patients aged 21 years and younger who were prescribed a GLP-1 RA from January 2015 to May 2024 at the Joslin Diabetes Center in Boston, Massachusetts. Results were reported during SCM25.

The primary end point of interest was the change in urine albumin-to-creatinine ratio (UACR) and eGFR from the time of initiation of the GLP-1 RA to discontinuation or final follow-up. The secondary outcome of interest was change in HbA1c. The Chronic Kidney Disease in Children U25 calculation was used to determine eGFR.

Of the 52 patients, 58% were female, 34% were Black, and 16% were Hispanic. Mean age at initiation of GLP-1 RA was 17.3 years, and duration of diabetes was 2 years. A total of 63 GLP-1 RAs were started (37 dulaglutide, 13 semaglutide, 7 liraglutide, and 6 tirzepatide). Forty-one patients had confirmed continuation. The median duration of GLP-1 RA use was 1.4 years.

After initiation of GLP-1 RA, there was a decrease in HbA1c from 9.5% to 8.6%; (P=0.04). No statistically significant changes were observed in UACR(9.6mg/gvs12.3mg/g;P=0.11)oreGFR(128mL/min/1.72m^2vs121mL/min/1.73 m^2; P=0.67).

In summary, the authors said. "Patients with YO-T2D demonstrate early signs of diabetes-related kidney disease with a third experiencing albuminuria. GLP-1 RA reduced HbA1c significantly in patients treated for at least 4 months. Studies with longer follow-up are needed to investigate the role that GLP-1 RA have on kidney outcomes in the youth."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-418. doi:10.1053/j.ajkd.2025.02.419

One-Year Results of the AFFINITY Study of Atrasentan in Patients With IgAN

The AFFINITY study (NCT04573920) is a phase 2, open-label basket trial of atrasentan in patients with kidney disease. The primary study end point was change in 24-hour UPCR from baseline to week 12. Atrasentan is a potent, selective endothelin A receptor antagonist used to treat IgAN and other kidney diseases. Researchers reported 1-year results during SCM25.

The study cohort included adults with biopsy-proven IgAN. Eligible participants had eGFR of 30 mL/min/1.73 m^2 or greater and UPCR 0.5 g/g or greater and less than 1 g/g, measured at the first morning void at screening and were receiving maximum tolerated/stable renin-angiotensin system inhibitors for 12 weeks or more. Patients received 0.785 mg oral atrasentan daily for 52 weeks.

Among 20 patients with IgAN, median age was 44.5 years, 50% were women, 45% were White, and 45% were Asian. Median 24-hour UPCR was 0.8 g/g; 12 patients had baseline UPCR of less than 1 g/g.

By week 6, there was an evident reduction in UPCR, which was sustained through week 52. In patients with baseline UPCR less than 1 g/g and in those with UPCR 1 g/g or greater, there were clinically meaningful reductions in UPCR through week 52. At baseline, week 12, and week 24, 5% (1 of 20), 60% (12 of 20), and 68% (13 of 19) of patients, respectively, had UPCR less than 0.5 g/g.

One patient discontinued treatment at week 13 due to a headache considered to be treatment related. No treatment-related serious adverse events or deaths were reported.

In summary, the researchers said, "Atrasentan was well tolerated and resulted in a stable, clinically meaningful reduction in proteinuria over 1 year of treatment, comparable between patients with baseline UPCR <1 and ≥1 g/g."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-447. doi:10.1053/J.ajkd.2025.02.448

Nephrologists' Perceptions of Reproductive Care for Women With Kidney Disease

Up to 3% of women of childbearing age have CKD, and those who are pregnant face considerable health risks. However, few data are available regarding nephrologists' perspectives on reproductive care for this population.

Researchers at the University of Cincinnati College of Medicine in Ohio conducted a survey to identify nephrologists' beliefs, practices, and perceived barriers to providing reproductive care for women with kidney disease. Results of the survey were reported at SCM25.

The 52-item electronic survey was sent to nephrologists across the United States. A total of 497 surveys were disseminated. Of those, 78 were available for evaluation (response rate of 16.3%). Median age of the surveyed nephrologists was 41 to 50 years; 53% were women, 83% practiced solely within an academic setting, and 53.7% had seen more than 15 women of childbearing age with kidney disease in the prior year.

Rates of initiating contraceptive discussions with female patients ranged from never (11%) to always (16%). Many respondents reported being "not at all confident" about managing sexual dysfunction (56.8%), menstrual disorders (42%), breastfeeding (24.7%), and contraception (13.6%). They most often cited the lack of standardized guidelines as a major barrier to providing reproductive care, followed by limited appointment time and lack of interdisciplinary coordination.

Rates of confidence with the issue of reproductive care were significantly higher among nephrologists who saw more than 15 women of childbearing age annually.

"Survey results indicate that a notable proportion of nephrologists in the United States express limited confidence and exhibit inconsistent practices in addressing reproductive health issues of sexual dysfunction and menstrual abnormalities with their female patients, with the absence of standardized guidelines emerging as a major obstacle to counseling. These findings underscore the need for a standardized approach and guidelines at a national level to guide reproductive care among women with kidney disease," the authors said.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-553. doi:10.1053/j.ajkd.2025.02.554

SPARTAN Trial Interim Results in Patients With IgAN

Interim results of the SPARTAN trial (NCT04663204), an open-label, single-arm, multicenter trial of sparsentan as first-line treatment for patients newly diagnosed with IgAN, were reported during SCM25.

The study cohort included 12 patients aged 18 years and older with biopsy-proven IgAN. Eligible patients had proteinuria of 0.5 g/d or greater and eGFR of 30 mL/min/1.73 m^2 or greater and had not used angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for 12 months or longer before study enrollment.

Study participants received sparsentan for 110 weeks, followed by a 4-week safety period. Proteinuria, BP, body weight, total body water (bioimpedance), urinary soluble CD163 (inflammatory biomarker), and safety were assessed.

Reductions in proteinuria were rapid: -61.9% by week 4 and sustained over 24 weeks. Complete proteinuria remission was seen in 58% of patients at any time during treatment. After an initial decrease, BP was stable over 24 weeks. Total body water and body weight were generally stable. Rapid and sustained reductions in urinary soluble CD163 were observed.

One patient discontinued treatment due to hypertension. The most frequent adverse event was dizziness.

"Sparsentan as first-line treatment was generally well tolerated, with reductions in proteinuria approximately 70% and urinary soluble CD163 approximately 50% over 24 weeks," the researchers said.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-452. doi:10.1053/j.ajkd.2025.02.453

SGLT2i Therapy and Changes in eGFR in US Veterans With ADPKD

SGLT2i therapy is used to delay the progression of CKD. However, few data on the efficacy of SGLT2i among patients with autosomal dominant polycystic kidney disease (ADPKD) are available.

Researchers conducted a study to examine the effects of SGLT2i on eGFR slope in patients with ADPKD and reported results at SCM25. The retrospective cohort study was conducted within the US Veterans Health Administration. The cohort included 348 adult patients with a diagnosis code for ADPKD who initiated treatment with an SGLT2i between January 2017 and May 2023.

The researchers evaluated eGFR slope before and after SGLT2i initiation using repeated-measures models. The effects of SGLT2i versus dipeptidyl peptidase-4 inhibition (DPP4i) on eGFR slope among patients with ADPKD and type 2 diabetes were compared using a target trial emulation.

Of 348 participants, 93% were male; mean age was 68 years, and median eGFR was 53 mL/min/1.73 m^2. In adjusted analyses, eGFR slope was -0.77 mL/min/1.73 m^2 before SGLT2i initiation, reduced to -2.89 mL/min/1.73 m^2 during the first 3 months after initiation, and attenuated to -0.18 during 3 to 12 months of follow-up.

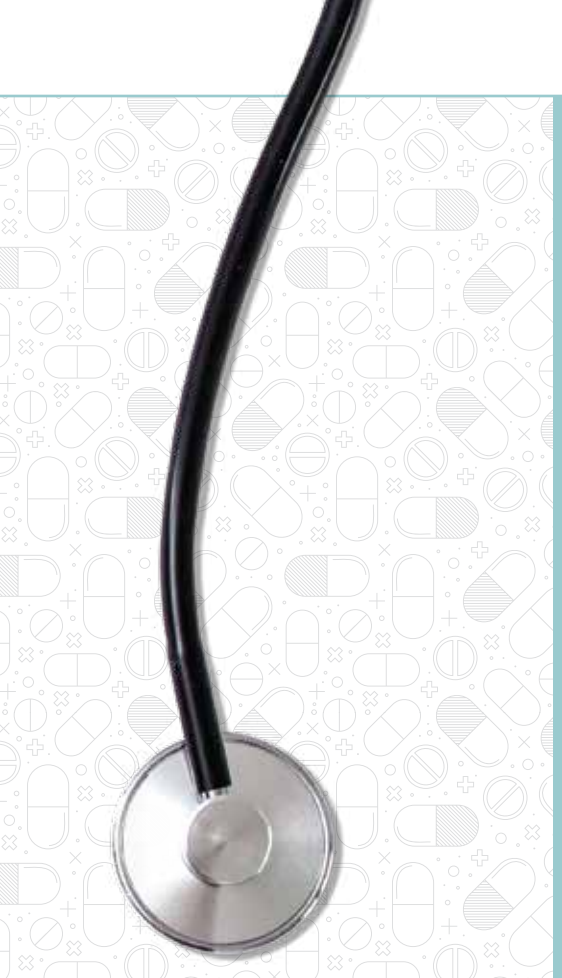
In the comparison model, during the first 3 months after SGLT2i use, eGFR declined -3.74 mL/min/1.73 m^2 days faster compared with DPP4i use. The slope was more stable among the SGLT2i users during 3- to 12-month follow-up (difference of 1.61 mL/min/1.73 m^2).

In conclusion, the authors said, "SGLT2i initiation in ADPKD was associated with steeper eGFR decline during the first 3 months post-initiation, followed by an attenuated eGFR slope for the remainder of the 1-year follow-up. In the subset of patients with type 2 diabetes, SGLT2i versus DPP4i use was associated with a slower eGFR decline between 3 to 12 months post-initiation. These findings suggest that SGLT2is are potentially beneficial in ADPKD, but further studies are required."

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #G-491. doi:10.1053/j.ajkd.2025.02.492

PRESSURE DROPS, RISKS RISE

Study Finds As-Needed BP Medications Increase AKI Risk



By Charlotte Robinson

Asymptomatic BP elevations are common occurrences among hospitalized patients, even those who do not have hypertension. Such occurrences are often treated with as-needed BP medications, including onetime and recurring as-needed administration. However, the benefits and consequences of this practice are unclear. Meanwhile, some research suggests there is an association between BP treatment and a higher risk of acute kidney injury (AKI) and other adverse outcomes.

With their study, **Muna Thalji Canales, MD,** and colleagues wanted to clarify whether treatment of asymptomatic BP elevations in the hospital with onetime or recurring use of as-needed medications increases the risk of AKI and other adverse outcomes.

The researchers conducted a retrospective cohort study of adults hospitalized for at least 3 days at Veterans Affairs hospitals between October 1, 2015, and September 30, 2020. Using target trial emulation, the researchers emulated a potential pragmatic randomized clinical trial comparing the impact of two approaches to treating inpatient hypertension (defined as at least one systolic BP reading of >140 mm Hg) on the development of AKI (defined as an increase in serum creatinine of 0.3 mg/dL from the baseline value within 48 hours or an increase by 50% over 7 days) and other secondary outcomes.

Participants were required to have been hospitalized in a medical or surgical unit other than the intensive care unit, not to have undergone surgery, and to have received at least one scheduled BP medication within the first 24 hours of hospital admission. Participants also must have had at least one systolic BP reading higher than 140 mm Hg during their hospitalization. Data were analyzed between April 2023 and August 2024.

Eligible participants were randomized to one of two approaches, either receiving as-needed BP medication (intervention arm) or as-needed BP medication not allowed (control arm). The retrospective study was designed to emulate the key elements of such a hypothetical trial.

The primary outcome was the onset of AKI after first use of as-needed BP medication or after the first scheduled BP medication administration. Secondary outcomes included a greater than 25% reduction in systolic BP within 3 hours of as-needed BP medication administration and the composite outcome of myocardial infarction, stroke, or death during hospitalization.

The analysis included assessment of key characteristics of veterans and their hospitalizations, which were considered as important for predicting as-needed BP medication administration and outcome development across comparison groups. An absolute standardized mean difference greater than 0.1 was considered a clinically consequential difference between comparison groups.

The researchers performed 1:1 exact matching between the groups on the reason for admission to minimize confounding by indication. Next, the propensity score was estimated using a logistic regression model (defined as the probability of as-needed BP medication exposure, given a set of observed covariates), and 1:1 propensity score matching was performed. Cox proportional hazard regression models were used to estimate hazard ratios (HRs) with 95% CIs for the time to first incidence of AKI and rapid BP reduction between as-needed BP medication recipients and matched control participants separately. In addition, several stratification analyses were conducted to examine the heterogeneity effects based on various factors.

The mean (SD) age of participants was 71.2 (11.6) years, 96% were male, 71.7% were White, 19.9% were Black, and 6.3% were Hispanic. Participants' mean (SD) baseline estimated glomerular filtration rate was 75.7 (22.7) mL/min/1.73 m^2.

A total of 133,760 veterans were included in the analysis. The as-needed BP medication group consisted of 28,526 patients (21%). However, 2,989 patients developed AKI before the first BP medication was administered. That left 130,771 patients for the AKI outcome analysis, of whom 26,202 (20%) received as-needed BP medication. Of patients included in the AKI outcome analysis who were receiving as-needed BP medications, 20,141 (80%) had onetime orders and 6,061 (20%) had as-needed orders. Eighteen percent received BP medications intravenously, 66% received BP medications orally, and 15% received both oral and IV medications.

In the primary analysis, after propensity score matching, AKI was 23% more likely to occur in patients who received at least one as-needed BP medication (HR, 1.23; 95% CI, 1.18-1.29) compared with those who did not. Subgroup analyses revealed a higher AKI risk with IV as-needed BP medication administration compared with oral or combined oral and IV administration. In the secondary analyses, patients receiving as-needed BP medications had a 1.5-fold greater risk of rapid BP reduction (95% CI, 1.39-1.62) and a 1.69-fold higher rate of the composite outcome (95% CI, 1.49-1.92) compared with patients not receiving as-needed BP medications.

The researchers acknowledge limitations of their study. There is a possibility of unmeasured or residual confounding, and some baseline values were missing. It is possible that some patients had symptoms that justified rapid BP reduction and that some patients received as-needed BP medications for reasons other than elevated BP. Other data regarding factors that could influence BP readings were limited. The use of the present-on-admission indicator with follow-up diagnosis codes to identify myocardial infarction or stroke may have led to biased ascertainment of outcomes. Lastly, the study's generalizability is limited.

In conclusion, the study found that use of as-needed BP medications for asymptomatic BP elevation in the hospital setting was associated with a higher risk of AKI, rapid decrease in BP, myocardial infarction, stroke, and death. The authors wrote, "The practical implication of our findings is that there is at least equipoise regarding the utility of as-needed BP medication use for asymptomatic BP elevations in hospitals. Thus, future prospective trials should evaluate the risks and benefits of this common practice." ●

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Canales MT, et al. *JAMA Intern Med.* 2025;185(1):52-60. doi:10.1001/jamainternmed.2024.6213

Pruritus During Dialysis Linked With High Risk for Adverse Health Outcomes

By Charlotte Robinson

Pruritus is a common symptom among patients with advanced chronic kidney disease (CKD), particularly those undergoing dialysis. Self-reported prevalence is 25% among individuals with nondialysis-dependent CKD and 40% among those receiving dialysis. The restlessness and discomfort that accompany pruritus make it a leading research priority for patients with advanced CKD.

However, characterization of pruritus burden is lacking, as is identification of populations at risk. Most previous research focuses on patients receiving hemodialysis (HD) rather than peritoneal dialysis (PD) and relies on self-reporting of symptoms.

Anne-Laure Faucon, MD, PhD, and colleagues studied a large cohort of patients receiving maintenance dialysis in Stockholm, Sweden, to quantify the population at risk for pruritus, their clinical determinants, and associated adverse health outcomes.

Their observational study incorporated data from the Stockholm Creatinine Measurement (SCREAM) study, a healthcare use cohort of the total population of the Stockholm area. The study included all patients initiating or receiving maintenance dialysis (HD or PD) from 2005 to 2021. The date of the first registered annual visit recorded in the Swedish Renal Registry was denoted as the index date (baseline) and the start of follow-up.

The study comprises two analyses. The outcome of the first analysis was clinically recognized pruritus, and the authors evaluated its prevalence, incidence, and primary baseline determinants. The second analysis considered pruritus to be a time-varying exposure and analyzed the association between prevalent or new-onset pruritus and a variety of adverse health outcomes (all-cause mortality, severe infection–related hospitalizations, de novo anxiety and depression, and sleep disorders).

The researchers assessed the baseline clinical determinants of prevalent pruritus using multivariable logistic regression. They used a multivariable cause-specific hazards model to evaluate new-onset pruritus overall and by dialysis modality. They then analyzed the association between pruritus and adverse health outcomes using time-varying cause-specific hazards models. Subgroup analyses were conducted to evaluate the consistency of results by age, sex, presence or absence of cardiovascular disease, diabetes, and dialysis modality. Sensitivity analysis was also performed.

A total of 3,281 patients receiving maintenance dialysis during 2005-2021 were identified. Of these patients, 77% had been receiving dialysis for less than 1 year at baseline. The median age of patients was 64 years, 66% were men, 69% were receiving HD, and the mean dialysis duration was 2.2 years.

At baseline, 456 (13.9%) patients had clinically recognized pruritus. Of those patients, 14.8% were receiving HD and 12.0% were receiving PD. *International Classification of Diseases, Tenth Revision (ICD-10)* codes were used to identify 36% of pruritus cases, and the other 64% were identified by initiation of pruritus treatment. Patients with pruritus were more often receiving HD, were older, were more likely to be women, and had a higher prevalence of cardiovascular disease, anxiety or depression, sleep disorders, and skin infections than patients without pruritus.

> This study highlights the prevalence of pruritus among patients receiving dialysis, identifies at-risk patient populations, and demonstrates that pruritus is linked to a high risk of adverse health outcomes.

Median follow-up was 3.3 years (interquartile range, 1.3-9.2), during which 539 (19.1%) patients who did not have pruritus at baseline (21.2% of patients receiving HD and 14.4% receiving PD) developed the condition. Total period prevalence of pruritus was 33%, and it was higher among patients receiving HD than those receiving PD (36.0% vs 26.4%; $P<0.01$). Overall, 19.3% of incident cases were identified through *ICD-10* codes, and the remainder were identified by initiation of pruritus treatment.

Clinical determinants of both prevalent and new-onset pruritus included older age; female sex; higher levels of C-reactive protein, serum calcium, and phosphate; and a lower level of serum albumin. Diabetes, however, was associated only with prevalent pruritus. Determinants were consistent across dialysis modality and dialysis vintage, although confidence intervals were broad.

During the follow-up period, 1,532 deaths, 949 infection-related hospitalizations, 328 new cases of anxiety or depression, and 485 new cases of sleep disorders occurred. Pruritus was not associated with the risk of all-cause mortality. However, pruritus was associated with higher risks of de novo anxiety and depression (adjusted hazard ratio [aHR], 1.56; 95% CI, 1.23-1.98) and sleep disorders (aHR, 1.96; 95% CI, 1.60-2.39) and with the risk of subsequent severe infections (aHR, 1.36; 95% CI, 1.18-1.57).

The results were consistent across subgroups by age, sex, diabetes, cardiovascular disease, and dialysis modality. Pruritus was associated with adverse health outcomes even when patients with prevalent pruritus at enrollment were excluded or the study population was limited to patients receiving incident dialysis. When pruritus was defined strictly by *ICD-10* codes or by initiation of pruritus treatment, similar trends occurred.

The authors acknowledge limitations of the study, including its observational nature, which may result in residual time-varying confounding; potential misclassification bias if pruritus is unreported or unrecognized or because medications for pruritus are nonspecific; and the lack of assessment of pruritus intensity and severity, the relationship between pruritus and the type of vascular access, and validation of the approach to identifying pruritus.

In summary, this study highlights the prevalence of pruritus among patients receiving dialysis, identifies at-risk patient populations, and demonstrates that pruritus is linked to a high risk of adverse health outcomes. The findings support periodic pruritus screening, particularly among high-risk patients, and personalized management, which may include "optimization of dialysis, treatment of CKD-associated mineral and bone disease, extemporaneous compounded topical preparations, systemic pharmacological treatments, UV therapy, and, in HD, difelikefalin, a recently introduced selective agonist of κ-opioid receptors." ●

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Accelerated Approval for Atrasentan in IgAN

By Charlotte Robinson

See Dr. Lafayette's interview–just scan the code.

Richard Lafayette, MD

In April, the FDA granted accelerated approval to atrasentan for the reduction of proteinuria in adults with primary IgA nephropathy (IgAN). Atrasentan, marketed by Novartis under the brand name Vanrafia, is an oral selective endothelin A receptor antagonist that may be used in conjunction with supportive care, such as renin-angiotensin system (RAS) inhibitors.

The approval was based on results of the phase 3 ALIGN study,[1] which showed that atrasentan achieved a proteinuria reduction of 36.1% ($P<0.001$) compared with placebo and had a favorable safety profile. *Nephrology Times* spoke with **Richard Lafayette, MD,** an ALIGN study investigator and steering committee member, about ALIGN, atrasentan, and the evolving landscape of IgAN treatments. Dr. Lafayette is also a professor of medicine and director of the Glomerular Disease Center at Stanford University Medical Center.

COULD YOU EXPLAIN THE MECHANISM OF ACTION FOR ATRASENTAN?

Atrasentan is a classic endothelin receptor antagonist. It blocks the endothelin 1 receptor, so it can block, downstream, all of those specific effects that endothelin has on its targets.

COULD YOU BRIEFLY CATCH US UP ON THE ALIGN STUDY? WHAT WERE THE KEY RESULTS OF THE 36-WEEK INTERIM ANALYSIS?

The ALIGN study was really designed to be an authoritative test of the role of endothelin blockade with atrasentan in IgA nephropathy. Blocking endothelin was purported to have multiple benefits because it acts both hemodynamically to reduce glomerular pressure, reduce proteinuria, but it also has multiple effects on other cell types including immune cells, resonant kidney endothelial cells, mesangial cells, and podocytes. It can be hemodynamically stabilizing, anti-inflammatory, and stabilizing to innate kidney cells.

It is really exciting to take this study forward. This was a randomized controlled trial of adult patients with IgA nephropathy who still had more than a gram a day of proteinuria, GFR [glomerular filtration rate] over 30 [mL/min/1.73 m^2], and were on maximally tolerated RAS inhibition and compared to placebo. The primary goal of the study was to show, at 9 months, that proteinuria would be statistically reduced in a clinically significant way, and then with the 2-year outcome plan, to show stabilization of kidney function compared to placebo.

In this part A, 9-month analysis, we have seen the data that there was indeed a statistically significant reduction of proteinuria in a way that should be quite clinically significant because the reduction of proteinuria was 38% and about 35% relative to the placebo group. It has been suggested by prior studies and meta-analysis to be clinically significant to predict the benefit to patients' long-term outcome.

THE 2-YEAR DATA WILL EVALUATE ESTIMATED GFR AND WHETHER ATRASENTAN SLOWS DISEASE PROGRESSION, CORRECT? WHAT DATA ARE STILL FORTHCOMING?

Correct. The FDA gets to see all the data for the patients, once that 9-month interim analysis is done on a large subset of the total population. But the 2-year data will explore, as a primary outcome, changes in kidney function by estimated GFR of the atrasentan group versus placebo. It will fill in further gaps about any subgroups.

It will look at sustainability of proteinuria and will also, very importantly, further comment on safety because, at the 9-month interval, we also saw a very nice safety record. Endothelin blockade in the past had been associated with some signals towards liver toxicity, towards volume retention, even bad enough to cause heart failure. But there were no signals towards liver toxicity in this study. There were only very mild and reversible signs of any fluid retention with no severe adverse events such as heart failure. We'll be able to further evaluate both the efficacy—that proteinuria reduction—look at subgroups, look at GFR stability as the primary outcome, and further evaluate safety. It will be very exciting to see further data.

THE LAST FEW YEARS HAVE BEEN EVENTFUL FOR IGAN DRUG DEVELOPMENT. WHERE DOES THE ACCELERATED APPROVAL OF ATRASENTAN FIT INTO THE TREATMENT LANDSCAPE?

It is really a beautiful, very exciting addition because... just a little over 2 years ago, we were really relying on RAS inhibitors to be our workforce for slowing progression of chronic kidney disease in IgA nephropathy patients. The evidence was that, even though they helped, they didn't do enough. Others relied on corticosteroids or systemic immunosuppression, which was associated with a substantial amount of adverse events and had a mixed record of efficacy.

Moving forward, now [we have] multiple agents that can target the galactose-deficient IgA production that underlies IgA nephropathy, further target potential antibodies against those galactose-deficient IgA, target the inflammation that might occur, such as using complement inhibitors, use dual endothelin antagonists together with angiotensin receptor antagonism. There are so many more options now that we really can tailor our therapy better to our patients.

A standalone endothelin antagonist like atrasentan is really very exciting to have in our toolbox because [for] patients who are doing well on their underlying therapy, but not quite at goal, this is really a great opportunity to get them exactly where we want in the hopes of really keeping their kidney function stable over the long run. So, it is just a very exciting, great addition. ●

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Obinutuzumab Shows Promise for Lupus Nephritis in Phase 3 Trial

By Charlotte Robinson

The REGENCY (NCT04221477) phase 3 trial demonstrated that obinutuzumab paired with standard therapy had greater efficacy than standard therapy alone in treating lupus nephritis. Study results from **Richard A. Furie, MD,** and colleagues were published in the *New England Journal of Medicine.*

Obinutuzumab is a humanized type 2 anti-CD20 monoclonal antibody that is approved to treat chronic lymphocytic leukemia and follicular lymphoma. In the previous NOBILITY trial, researchers compared obinutuzumab plus standard therapy (mycophenolate mofetil and glucocorticoids) with standard therapy alone among patients with lupus nephritis.

They found that obinutuzumab use, compared with placebo, resulted in clinically meaningful improvements among patients with a complete renal response at 52, 76, and 104 weeks. In addition, the drug prolonged the time to a lupus nephritis flare and an unfavorable kidney outcome (a composite of treatment failure, doubling of the serum creatinine level, or death). Treatment with obinutuzumab also lessened estimated glomerular filtration rate (eGFR) decline compared with placebo.

[T]he addition of obinutuzumab to standard therapy led to a significantly greater percentage of patients with a complete renal response at week 76 than standard therapy alone.

Following up on those results, REGENCY assessed the efficacy and safety of obinutuzumab plus standard therapy among a population with active, proliferative lupus nephritis. The randomized, double-blind, placebo-controlled trial was carried out in 15 countries and included 271 adults.

Participants were aged 18 to 75 years; met American College of Rheumatology classification criteria for systemic lupus erythematosus; and had active class 3 or 4 lupus nephritis with or without concomitant class 5 disease (according to the International Society of Nephrology and the Renal Pathology Society), biopsy-confirmed during screening or within 6 months. In addition, participants had 24-hour urine protein to creatine ratio (UPCR) of 1 mg/mg or higher and antinuclear antibody (ANA) positivity (an ANA titer of ≥1:80 on HEp-2 cells or ≥1 equivalent positive ANA test result).

Patients were randomized 1:1 to receive either IV infusions of obinutuzumab (n=135) or placebo (n=136). Obinutuzumab was administered on one of two dose schedules: 1,000 mg on day 1 and at weeks 2, 24, 26, and 52, with or without an additional dose at week 50.

Of all participants, 14.8% were Black or African American, 5.9% were Asian, and 57.6% were Hispanic or Latino. In the obinutuzumab group, the mean (SD) patient age was 33.0±10.5 years and 84.4% were women. In the placebo group, the mean (SD) patient age was 32.7±10.0 years and 84.6% were women. In the obinutuzumab group, the mean eGFR was 102.8±29.3 mL/min/1.73 m^2 and mean UPCR was 3.14±2.99 mg/mg. In the placebo group, the mean eGFR was 101.9±32.2 mL/min/1.73 m^2 and the mean UPCR was 3.53±2.76 mg/mg.

Among participants with previously diagnosed lupus nephritis (obinutuzumab group: n=81; placebo group: n=76) versus those who were newly diagnosed, the median duration since the first lupus nephritis diagnosis was 36.6 months (range, 0.4-330.4) for the obinutuzumab group and 34.3 months (range, 0.8-217.8) for the placebo group.

The primary end point of the study was a complete renal response at week 76; this was defined as 24-hour UPCR lower than 0.5 mg/mg; eGFR at least 85% of baseline value; and no occurrence of an intercurrent event (rescue therapy, treatment failure, death, or early trial withdrawal). Secondary end points included a complete renal response with a prednisone dose of 7.5 mg/day or lower between weeks 64 and 76 and a UPCR lower than 0.8 mg/mg without an intercurrent event at week 76.

At week 76, a complete renal response was seen in 46.4% of participants in the obinutuzumab group compared with 33.1% in the placebo group (adjusted difference, 13.4 percentage points; 95% CI, 2.0-24.8; *P*=0.02). The placebo group had a higher percentage of patients with treatment failure (17.6%) compared with the obinutuzumab group (3.7%). Similarly, the placebo group had a higher percentage of patients receiving rescue therapy compared with the obinutuzumab group (17.6% vs 5.9%).

A complete renal response between weeks 64 and 76 with a prednisone dose of 7.5 mg or lower occurred in 42.7% of the patients in the obinutuzumab group and 30.9% in the placebo group (adjusted difference, 11.9 percentage points; 95% CI, 0.6-23.2; *P*=0.04). At week 76, the percentage of participants with a UPCR lower than 0.8 mg/mg with no intercurrent event was 55.5% in the obinutuzumab group and 41.9% in the placebo group (adjusted difference, 13.7 percentage points; 95% CI, 2.0-25.4; *P*=0.02)

An exploratory analysis using the primary end point, but with death as the only intercurrent event, yielded results consistent with the primary analysis. Results of prespecified subgroup analyses were mostly consistent across the subgroups, including patients with class 4 lupus nephritis, concomitant class 5 lupus nephritis, a baseline UPCR of 3 mg/mg or higher, or serologic activity.

The percentage of participants who experienced adverse events was comparable in the obinutuzumab (92.6%) and placebo groups (88.6%). More serious adverse events occurred in the obinutuzumab group (32.4%) than in the placebo group (18.2%). The most common serious adverse events among the obinutuzumab group participants were infections.

The authors concluded that, "In this trial involving adults with biopsy-proven active lupus nephritis, the addition of obinutuzumab to standard therapy led to a significantly greater percentage of patients with a complete renal response at week 76 than standard therapy alone." ●

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Effect of Sotagliflozin on Hemoglobin in Patients With CKD and T2D

By Charlotte Robinson

Anemia is a common complication of chronic kidney disease (CKD) that is associated with adverse kidney and cardiovascular (CV) outcomes. Erythropoietin-stimulating agents and hypoxia-inducible factor prolyl hydroxylase inhibitors have been used for anemia management, but both are associated with CV risks.

Sodium-glucose cotransporter (SGLT) inhibitors are known to increase hemoglobin while improving cardiorenal outcomes. The subject of this analysis was the dual SGLT1 and SGLT2 inhibitor sotagliflozin. **Vikas S. Sridhar, MD,** and colleagues analyzed the agent's effects on hemoglobin in patients with stage 3 or 4 CKD and type 2 diabetes (T2D) with and without anemia.

The researchers conducted a post hoc analysis of pooled participant-level data from two clinical trials over 26 weeks involving participants with CKD stages 3 or 4 and T2D. Using an analysis of covariance, the researchers compared the change in hemoglobin from baseline between sotagliflozin 200 mg or 400 mg and placebo in the pooled cohort, adding CKD study as a fixed variable.

Clinical factors associated with hematopoiesis, such as baseline estimated glomerular filtration rate (eGFR), use of anti-anemic preparations, and use of renin-angiotensin system (RAS) inhibitors were covariates in a sensitivity analysis.

The researchers identified participants with anemia at baseline based on hemoglobin levels of less than 13 mg/dL for men and less than 12 mg/dL for women. They evaluated the change from baseline in hemoglobin, hematocrit, serum albumin, systolic BP, body weight, and eGFR between sotagliflozin (pooled dose) and placebo in participants with and without anemia. Sotagliflozin doses were pooled for the anemia subgroup analyses because hemoglobin changes were similar between doses.

A total of 1,064 participants were included in the analysis, of whom 493 (46.3%) had anemia at baseline. Of the anemia group, 228 (46%) were female, 396 (80%) were White, 40 (8%) were Black, and 172 (35%) were Hispanic/Latino. The mean (SD) age was 68 (9) years. The participants with anemia had a lower mean [SD] baseline eGFR compared with those without anemia (36 [12] mL/min/1.73 m^2 vs 43 [11] mL/min/1.73 m^2). A larger percentage of these participants had CKD stage 4 (37% vs 17%) and moderately increased albuminuria (69% vs 53%).

The no anemia group comprised 571 individuals, of whom 257 (45%) were female, 497 (87%) were White, 11 (2%) were Black, and 133 (23%) were Hispanic/Latino. The mean age was 70 (8) years.

Over 26 weeks, the effects of sotagliflozin on hemoglobin when compared with placebo were similar regardless of whether participants had anemia (*P* interaction=0.062). Sotagliflozin increased hemoglobin in a rapid and lasting manner for both groups. Compared with placebo, sotagliflozin increased mean hemoglobin level by 0.27 g/dL among participants with anemia and by 0.50 g/dL in participants without anemia.

Within the full cohort, the baseline mean hemoglobin level was 12.7 g/dL. Sotagliflozin increased hemoglobin by 0.39 g/dL with the 200-mg dose (95% CI, 0.21-0.56) and 0.41 g/dL with the 400-mg dose (95% CI, 0.24-0.59) compared with placebo (*P*<0.001) from baseline to week 26. In the sensitivity analysis adjusted for baseline eGFR, use of anti-anemic preparations, and use of RAS inhibitors, the placebo-adjusted increase in hemoglobin for the pooled dose of sotagliflozin was 0.43 g/dL (95% CI, 0.26-0.59; *P*<0.001).

Among participants who had anemia at baseline, sotagliflozin increased the likelihood of their anemia resolving over the 26-week follow-up period (odds ratio [OR], 1.95; 95% CI, 1.13-3.37; *P*=0.017). Among participants without anemia at baseline, there was a decrease, although nonsignificant, with sotagliflozin in their odds of developing anemia over 26 weeks (OR, 0.75; 95% CI, 0.39-1.47; *P*=0.41).

Participants without anemia had greater placebo-adjusted reductions in blood pressure and body weight compared with participants without anemia (*P* interaction <0.05). The safety and tolerability of sotagliflozin were similar between the two anemia subgroups and were consistent with expectations in patients with T2D and CKD.

The authors noted a few limitations of their study. Because of the short follow-up period, it could not be determined whether changes in hemoglobin with sotagliflozin are lasting or are associated with clinically meaningful outcomes. Sotagliflozin works by mechanisms similar to those of other SGLT inhibitors that have been shown to increase erythropoietin and iron metabolism, but details regarding how it affects hemoglobin are lacking due to the absence of data on markers of erythropoiesis.

In summary, the authors wrote, "Sotagliflozin increased haemoglobin in patients with T2D and CKD, supporting its potential use in the management of anaemia in this population, in addition to known cardiorenal protective effects." ●

Over 26 weeks, the effects of sotagliflozin on hemoglobin when compared with placebo were similar regardless of whether participants had anemia.

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Phase 3 TRANSCEND Study Will Evaluate Use of Felzartamab for AMR

By Charlotte Robinson

Biogen recently announced the initiation of TRANSCEND (NCT06685757), a phase 3 study of felzartamab for the treatment of late antibody-mediated rejection (AMR) after kidney transplant. Antibody-mediated rejection affects approximately 23,000 US patients and is a leading cause of kidney transplant loss.

Suphamai Bunnapradist, MD

Felzartamab is an investigational therapeutic human monoclonal antibody directed against CD38, a protein expressed on mature plasma cells.

Nephrology Times spoke with **Suphamai Bunnapradist, MD,** professor of clinical medicine at the David Geffen School of Medicine and research director of the Connie Frank Kidney Transplant Center at UCLA, who is the principal investigator of the study.

COULD YOU GIVE AN OVERVIEW OF THE STUDY OF FELZARTAMAB FOR AMR?

So, we're excited. We are looking at a phase 3 study—that has a really interesting phase 2 result—to look for treatment of chronic late antibody-mediated rejection, which we know is a leading cause of graft failure in the long run. As of now, there's no treatment for it. What we believe is, the antibody-mediated rejection—a lot of study has been ongoing and has been done that [looks] at how to reduce the effect of antibody by removing [the] antibody itself, use medication to remove the cells that produce [the] antibody, or treat the effect of the antibody through the complement- and non–complement-mediated pathways.

In this particular study, the anti-CD38 is used to address plasma cells and natural killer cells. And the phase 2 study that was published in the *New England Journal of Medicine*[1] showed a very good, dramatic result in reducing MVI [microvascular inflammation] from 80% in patients who got the drug to 20% in those that did not get the drug. And therefore, we're going to be starting a global phase 3 study of 120 patients. So, it's exciting. We still have to go to the trial, and I'm hopeful that this may lead to a new effective treatment for our patients that is very much needed.

HOW DOES FELZARTAMAB WORK? WHAT SETS IT APART FROM OTHER THERAPIES?

This is very interesting, because when we talk about AMR, or antibody-mediated rejection, we think the culprit is the antibody. So, in order to deplete the antibody, we have been, in history, trying to remove antibody, use the drug that we know would deplete antibody, and this particular drug is directed against a molecule called CD38, which basically is on the surface of the plasma cell. So, the idea is we kill the plasma cells, and we then deplete the antibody.

EXPLAIN THE STUDY DESIGN AND OUTCOMES FOR THE PHASE 3 STUDY.

The phase 3 study looks at the patients who have antibody-mediated rejection that is chronic. They include patients who are more than 6 months from the transplant. The new definition of antibody-mediated rejection includes basically two groups: one group is you identify HLA antibody in the blood, and the other group is, they may not have antibody that you can detect in the blood, but you have evidence of antibody injury by evidence of C4d positivity in the tissue. This part of the study, this study's looking at patients who have to have both HLA antibody and evidence of the antibody rejection. They cannot have concurrent significant cellular rejection, and they have to have reasonable kidney function. So, that's the inclusion criteria of the study.

With that, we are looking at recruiting 120 patients, and the way the study design works is 2:1 randomization. [With] the randomization, two-thirds would get the medication right away, one-third would serve as a control group, did not get the medication. They would get medication or placebo for a total of 6 months. At 6 months, they would be rolled over. The group that did not get the medication would get the medication at 6 months. In other words, two-thirds get the medication for 6 months, [and] one-third didn't get it; at 6 months, they will get the medication.

They'll be doing two biopsies, one at 6 months and one at 1 year—that would be the end of the study—to look at the efficacy in terms of the resolution of the antibody-mediated rejection. The other thing that is important to note is they cannot receive any other treatment for antibody-mediated rejection. That is, they cannot receive intravenous immunoglobulin (Ig), which we use, or rituximab that we use. I should note that the IV Ig or the rituximab is not indicated for treatment of chronic antibody-mediated rejection at this time, and there's no evidence that they would improve chronic antibody-mediated rejection. And the most important thing I would say is, at this point we don't have effective treatment for antibody-mediated rejection. ●

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Prefer to watch?
Scan the code to see
Dr. Bunnapradist's interview.

Novartis to Acquire Kidney-Focused Biotech Regulus Therapeutics

Regulus Therapeutics, a biopharmaceutical company based in San Diego, California, announced that it will be acquired by Novartis.

Regulus is focused on discovering and developing medicines targeting microRNAs. Its leading product candidate is farabursen, a novel oligonucleotide for the treatment of autosomal polycystic kidney disease (ADPKD) designed to inhibit miR-17 and to preferentially target the kidney.

"With limited treatment options currently available for patients suffering from ADPKD, farabursen represents a potential first-in-class medicine with a profile that may provide enhanced efficacy, tolerability, and safety versus standard of care," **Shreeram Aradhye,** president of development and chief medical officer of Novartis, said in a statement.

The acquisition is expected to be completed in the second half of 2025.

Source: Regulus Therapeutics.

EU Approves Sparsentan for Treatment of IgAN

Travere Therapeutics and CSL Vifor announced that the European Commission has granted standard approval to sparsentan for the treatment of adults with primary IgA nephropathy (IgAN) with a urine protein excretion of 1.0 g/d or higher or a urine protein-to-creatinine ratio of 0.75 g/g or higher.

The drug, which is marketed under the brand name Filspari, was previously granted conditional marketing approval. The conversion to standard marketing authorization applies to all members of the European Union, Iceland, Liechtenstein, and Norway.

The decision was supported by data from the phase 3 PROTECT study, which compared sparsentan, a dual endothelin angiotensin receptor antagonist, with the angiotensin receptor blocker irbesartan. After 36 weeks of treatment, patients receiving sparsentan achieved a mean reduction in proteinuria from baseline of 49.8% versus 15.1% with irbesartan. Two-year confirmatory results demonstrated that sparsentan significantly slowed kidney function decline when compared with irbesartan.

Conditional approval of sparsentan for IgAN in the United Kingdom was converted to standard approval effective April 15, 2025. The drug received full approval for the treatment of IgAN in the United States in September 2024.

Source: Travere Therapeutics.

ASN to Launch Centers of Excellence in Home Dialysis Pilot Program

The American Society of Nephrology (ASN) announced that it will create a Centers of Excellence in Home Dialysis pilot program to recognize healthcare organizations meeting or exceeding national standards and guidelines for home dialysis care. The program is intended to increase access to home dialysis, strengthen home dialysis programs, and improve patient outcomes.

"Through this ASN program, designated facilities can serve as a model for home dialysis care and demonstrate their commitment to ensuring choice of modality treatment for all people with kidney diseases," **Edward Gould, MD,** co-chair of the ASN Home Dialysis Steering Committee and chair of the Centers for Excellence in Home Dialysis Workgroup, said in a statement. "By setting criteria for programs to be considered excellent, clinicians and organizations can strive for excellence and those with the award can become recognized as regional leaders in home dialysis, serving as a resource to other home dialysis clinicians and programs."

At the start of the Medicare End-Stage Renal Disease (ESRD) Program in 1973, more than 40% of patients receiving dialysis did so in a home setting. That percentage had dropped to 13.1% by 2019, although the number of US patients receiving dialysis had grown from about 11,000 to 566,614.

Currently, about 14.5% of US patients receive dialysis at home. Despite the modest increase, barriers to home dialysis remain, including fear, lack of awareness, lack of infrastructure, lack of workforce training, and staff shortages.

Source: American Society of Nephrology.

FDA Approves Lupin's Generic Tolvaptan Tablets

Drug maker Lupin Limited announced that the FDA approved an Abbreviated New Drug Application for its generic tolvaptan 15 mg, 30 mg, 45 mg, 60 mg, and 90 mg tablets. As the exclusive first-to-file for this drug, the company is eligible for 180 days of generic drug exclusivity.

The FDA approved tolvaptan in April 2018 to slow kidney function decline in adults at risk for rapidly progressing ADPKD. It is the first approved treatment for ADPKD, which is the fourth leading cause of end-stage renal disease. The drug is currently marketed by Otsuka under the brand name Jynarque.

Lupin CEO **Vinita Gupta** said in a statement, "We are very pleased to have obtained approval for generic Tolvaptan from the US FDA. This marks a significant entry into the nephrology segment and demonstrates our commitment to addressing the unmet needs of patients globally."

The generic tolvaptan tablets will be manufactured in Nagpur, India.

Sources: Lupin, Otsuka.

KDIGO Publishes Updated Guideline on Nephrotic Syndrome in Children

Kidney Disease: Improving Global Outcomes (KDIGO) issued a new, updated guideline on the management of nephrotic syndrome in children. The previous guideline update was published in 2021.

In an executive summary published in *Kidney International,* the authors noted the significant addition of a treatment algorithm providing details on when to perform a kidney biopsy and/or genetic testing and which immunosuppressive therapy to prescribe for children with a complete response to glucocorticoids who experience infrequent or frequent relapses or become steroid dependent.

Another notable change is that various clinical scenarios have been defined to align with the International Pediatric Nephrology Association guideline on the management of children with steroid-sensitive and steroid-resistant nephrotic syndrome.

The full guideline is available on KDIGO's website at kdigo.org/guidelines/nephrotic-syndrome-in-children.

Source: Floege J, et al. *Kidney Int.* 2025;107(5):806-808. doi:10.1016/j.kint.2024.11.006

ACUTE KIDNEY INJURY

Using Serum Cystatin C in Diagnosis of AKI

Clin J Am Soc Nephrol. doi:10.2215/CJN.0000000654

A significant proportion of hospitalized and critically ill patients experience acute kidney injury (AKI). Serum creatinine (sCr) is the measurement used to diagnose AKI. However, there are known limitations associated with the use of sCr that affect the timely detection and response to the management of patients with AKI. Those limitations may be overcome with the use of serum cystatin C (sCys) levels. According to **Levi Hooper, PharmD,** and colleagues, there are few data available on direct comparisons of those biomarkers in AKI diagnoses.

Using Matrix Laboratories and Simbiology (The MathWorks, Natick, Massachusetts), the researchers developed a quantitative systems pharmacology model to simulate the concentration-time profiles of sCr and sCys under varying degrees of AKI across a spectrum of baseline kidney function. Parameters from existing literature and a contemporary sCr and sCys glomerular filtration rate (GFR) equation were used to assess the time to reach AKI diagnostic criteria for both biomarkers.

Analysis results demonstrated that sCys achieved steady-state concentration and met the threshold for AKI diagnosis significantly faster than sCr, with an advantage of 6 to 48 hours depending on the stage of chronic kidney disease (CKD). Sensitivity in detection of GFR reductions was greater with sCys, with the ability to detect AKI within 12 to 14 hours following onset, compared with 12 to 72 hours for sCr. In addition, for sCys the absolute value diagnostic cutoffs were more effective than the threshold based on percentage, providing consistent detection across varying stages of CKD.

In summary, the authors said, "sCys has superior kinetics for early AKI detection compared with sCr, making it a valuable addition to AKI diagnostic protocols, particularly in high-risk populations. Daily monitoring of sCys in patients at risk of AKI would facilitate more timely detection and potentially improve clinical outcomes. Further research should focus on validating sCys diagnostic criteria and integrating it with other biomarkers to enhance AKI management."

ADPKD

Long-Term Efficacy of Tolvaptan in ADPKD

Nephrol Dial Transplant. doi:10.1093/ndt/gfaf048

At present, tolvaptan is the only therapy available to improve disease progression in patients with autosomal dominant polycystic kidney disease (ADPKD). Tolvaptan is a vasopressin V2 receptor antagonist. There are few data available on real-life outcomes with tolvaptan, and previous study findings are limited by small study sizes, short follow-up periods, or lack of control groups.

Paul Geertsema, MD, and colleagues conducted a study designed to examine the long-term effect of tolvaptan on kidney function and growth in patients with ADPKD compared with controls. The study also assessed determinants of long-term treatment efficacy. The control group included patients with ADPKD who were not treated with tolvaptan.

The study utilized pooled data from the prospective DIPAK cohort and the retrospective OBSERVA cohort. Researchers measured total kidney volume (TKV) every 3 years and estimated GFR (eGFR) yearly. Acute slope end points were analyzed as treatment effects from tolvaptan initiation to 6 weeks, and chronic slope end points were analyzed following the initial 6 weeks of treatment.

The total analysis cohort included 615 patients; of those, 105 were treated with tolvaptan. The mean age in the overall cohort was 48 years, and 58.2% were female. The average duration of treatment was 6.1 years. The matched analysis cohort included 92 patients in each group (treated and non-treated).

During chronic slope, there was a 14.0% decline in eGFR (–4.36 to –3.75 mL/min/1.73 m^2/year; P=0.03) in the tolvaptan group compared with a decrease of 1.0% (–4.16 to –4.12 mL/min/1.73 m^2/year; P=0.9) in the control group. There was no significant change in long-term TKV growth during the tolvaptan treatment period. The tolvaptan treatment effect was greater among a subgroup of patients with a higher mean osmolar intake.

"In this study, with real-life patient data, long-term follow-up, and a well-matched control group, we found that tolvaptan attenuated long-term kidney function decline but seemed not to influence kidney growth," the researchers said.

Race and Transplantation Outcomes Among Patients With ADPKD

Clin J Am Soc Nephrol. doi:10.2215/CJN.0000000626

ADPKD is the most common genetic cause of end-stage kidney disease (ESKD), and it occurs without racial predilection. Generally, patients in racial and ethnic minority groups with ESKD have limited access to kidney transplantation, particularly living donor transplantation. **Sambhavi Krishnamoorthy, MBBS,** and colleagues conducted a study examining long-term outcomes of patients with ADPKD-associated ESKD by self-reported race, with an emphasis on the trajectory of estimated post-transplant survival (EPTS) scores over time.

Using data from the United Network for Organ Sharing Standard Transplant Analysis and Research files, the researchers identified 32,611 ADPKD transplant recipients from January 2000 to December 2022. The time from the date of waitlisting to transplant was used to calculate EPTS scores. The cumulative incidences of living and deceased donor transplants were calculated and plotted, and Cox models were made for graft failure and death. A subdistribution hazards model for graft failure accounted for death as a competing outcome, with adjustments for patient, donor, and transplant factors.

Compared with White patients with ADPKD, all other groups had longer dialysis duration, more delayed graft function, and fewer living and preemptive transplants. At each point on the waitlist, Black and Hispanic patients had lower mean EPTS scores compared with White patients. Due to longer waiting times, EPTS scores were less likely to be less than 20% in Black and Hispanic patients at the time of transplant.

Compared with White patients, the risk for graft failure with death as a competing risk was significantly higher in Black patients. Graft survival was similar among Asian and Hispanic patients; patient survival was better among Asian and Hispanic patients compared with White patients.

In conclusion, the researchers said, "Waitlist experience, allograft quality, and post-transplant outcomes of patients with ADPKD are influenced by patient race."

ANCA-ASSOCIATED VASCULITIS

Minimizing Glucocorticoid Use in Patients With ANCA-Associated Vasculitis

Kidney Int Rep. doi:10.1016/j.ekir.2025.04.030

There are few data available regarding the optimal duration of immunosuppressive therapy for antineutrophil cytoplasm antibody (ANCA)–associated vasculitis (AAV). Current treatment includes glucocorticoids; however, the use of those agents is associated with significant morbidity.

Tania Salehi, MBBS, and colleagues conducted a retrospective, observational cohort study examining outcomes among patients who presented with AAV from 2011 to 2013 and who were treated with combination cyclophosphamide and rituximab induction in tandem with a rapidly tapering oral-only glucocor-

ticoid regimen. The researchers analyzed biochemical, histologic, and outcome data, including time to remission and rate of relapse.

The cohort included 112 eligible patients; the mean age was 67 years, 85% had kidney involvement, and the mean baseline eGFR was 24 mL/min/1.73 m^2. Ninety-six percent of the cohort achieved remission, with a median time to remission of 77 days. Improvement in biochemical and histological values was observed following treatment in all patients. Five patients experienced a disease relapse over 2.9 years of follow-up.

The cumulative dose of glucocorticoid was 1,780 mg with a median duration of 12 weeks. The cumulative dose was higher in patients who were treated with oral glucocorticoids for more than 12 weeks (2,935 mg vs 1,133 mg; $P<0.001$), with a trend toward more serious infections compared with patients treated for 12 weeks or less (21% vs 7%; $P=0.06$). There were no differences in disease remission (100% vs 91%; $P=0.07$) or relapse (9% vs 0%; $P=0.07$) between the two groups.

In summary, the authors said, "Early withdrawal of oral glucocorticoid therapy in patients with severe AAV treated with combination cyclophosphamide and rituximab induction immunosuppression is safe and effective and may reduce morbidity, in particular, serious infections."

CHRONIC KIDNEY DISEASE

Treatment Effects on Acute and Chronic GFR Slope in Clinical Trials

Clin J Am Soc Nephrol. doi:10.2215/CJN.0000000662

Trials among patients with CKD use GFR slope as a validated surrogate end point. However, due in part to the inability to separate distinct contributions of the acute (before 3 months) and chronic (after 3 months) slopes for treatment effects on clinical end points, ambiguities may exist regarding the appropriate period for slope evaluation.

Tom Greene, PhD, and colleagues utilized data of 66 randomized treatment comparisons from previous CKD trials to estimate treatment effects on the acute and chronic GFR slopes and on the established clinical end point of kidney failure or serum creatinine doubling. To determine the independent contributions of the acute and chronic slopes, the researchers used a Bayesian meta-regression framework to relate treatment effects on the established clinical end point to both slopes.

The model suggested that treatment effects on both the acute and chronic slopes were independent predictors of the treatment effect on the established clinical end point, with a high median R^2 of 0.95. For a fixed treatment effect on the chronic slope, each 1 mL/min/1.73 m^2 greater acute GFR decline for the treatment versus control group increased the hazard ratio (HR) for the established clinical end point by 11.4% against the treatment. The 3-year total slope was defined as the average slope extending from baseline to 3 years; the optimal weights for the acute and chronic slopes were consistent with the 3-year total slope.

"Treatment effects on both the acute and chronic GFR slopes are independent determinants of the effects on the established clinical end point, with variation in acute effects accounting for much of the observed variation in treatment effects on the clinical end point across previous trials," the researchers said. "Our results establish that acute effects impact the clinical end point independently of treatment effects on the chronic slope and support the 3-year total slope as the primary slope-based outcome in randomized trials."

Ischemic Cardiovascular Outcomes Improved With Dual SGLT Inhibitor

Lancet Diabetes Endocrinol. doi:10.1016/S2213-8587(24)00362-0

The benefit in improving heart failure–related outcomes with sodium-glucose cotransporter (SGLT)-2 inhibitors is well established. However, there are few data available on the benefit of those agents in ischemic cardiovascular events such as myocardial infarction or stroke. **Rahul Aggarwal, MD,** and colleagues performed a prespecified secondary analysis of the SCORED trial to assess whether sotagliflozin, a dual SGLT-1/2 inhibitor, improves outcomes for patients experiencing ischemic cardiovascular events.

The trial cohort included adult patients with type 2 diabetes, CKD (eGFR 25-60 mL/min/1.73 m^2), and additional cardiovascular risk factors at 750 sites in 44 countries. Participants were randomly assigned 1:1 to oral sotagliflozin 200 mg once a day, increased to 400 mg once a day within 6 months if tolerated, or placebo. A prespecified secondary outcome was total major adverse cardiovascular events (MACE), defined as a composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.

A total of 10,584 patients were enrolled (sotagliflozin: n=5,292; placebo: n=5,292). Median age of the overall cohort was 69 years, 44.9% were female, 48.6% had a history of myocardial infarction, 8.9% had a history of stroke, and 22.4% had a history of coronary revascularization. The rate of total MACE was significantly lower among patients in the sotagliflozin group than in the placebo group (4.8 events per 100 person-years vs 6.3 events per 100 person-years; HR, 0.77; 95% CI, 0.65-0.91; $P=0.002$).

Results of interaction analyses among groups stratified by baseline demographic and clinical features, heart-related criteria, eGFR, urine albumin-creatinine ratio, and history of cardiovascular disease suggested a consistent effect of sotagliflozin in total MACE without evidence of heterogeneity. The rates of myocardial infarction and stroke were reduced compared with placebo.

"Sotagliflozin reduced MACE, with independent reductions in myocardial infarction and stroke, among patients with type 2 diabetes, chronic kidney disease, and additional cardiovascular risk. The ischemic benefit on myocardial infarction and stroke has not been previously observed with other SGLT inhibitors and warrants investigation of combined SGLT1 and SGLT2 inhibitors as a possible underlying mechanism," the authors said.

CKM SYNDROME

Risk of Cardiovascular Mortality Varies With CKM Stage

J Am Soc Nephrol. doi:10.1681/ASN.0000000637

Evaluation of the prognostic implications of the staging of cardiovascular-kidney-metabolic (CKM) syndrome is key in informing clinical practice. **Sophie E. Claudel, MD,** and colleagues conducted a study designed to define the mortality risk associated with each stage of CKM syndrome and identify the corresponding restricted mean survival time over a period of 15 years.

The longitudinal study included 50,678 community-dwelling US adults aged 20 years or older. Eligible patients had available baseline data for CKM stage determination and participated in the 1999 to 2018 National Health and Nutrition Examination Survey. The American Heart Association presidential advisory criteria were used to define CKM stages. Confounder-adjusted survival curves using the G-formula were used to calculate 15-year adjusted cumulative incidences of cardiovascular mortality.

The median follow-up was 9.5 years. During the follow-up period, there were 2,565 cardiovascular deaths. Stratified by stages of CKM, the 15-year adjusted cumulative incidences of cardiovascular mortality were: stage 0, 5.5% (95% CI, 1.8-9.3); stage 1, 5.7% (95% CI, 3.2-8.2); stage 2, 7.9% (95% CI, 6.8-9.1); stage 3, 8.7% (95% CI, 6.7-10.8), and stage 4, 15.2% (95% CI, 13.6-16.8).

At 15 years, the absolute risk difference between CKM stage 4 and CKM stage 0 was 9.6% (95% CI, 5.6-13.6), and the survival difference between CKM stage 0 and CKM stage 4 was 8.1 (95% CI, 8.0-8,2) months.

"Our findings reveal a graded risk of cardiovascular mortality associated with higher CKM syndrome stage," the researchers concluded.

DIABETES

Outcomes With Finerenone Among Patients With Acute Changes in eGFR

Kidney Int. doi:10.1016/j.kint.2025.03.018

Using prespecified pooled patient data from the FIDELITY trial, **Sankar D. Navaneethan, MD, MPH,** and colleagues sought to assess the efficacy and safety of finerenone according to different changes in eGFR compared with placebo. Finerenone is a non-steroidal mineralocorticoid receptor antagonist.

Eligible patients had CKD, defined as an eGFR of 25 mL/min/1.73 m^2 or greater, and type 2 diabetes with optimized renin-angiotensin system blockade. Change in baseline eGFR at 1 month in the total study cohort and by treatment group was used to analyze the risk of composite cardiovascular and composite kidney outcomes.

The overall cohort included 12,796 patients. Over 1 month of treatment, 25.1% of patients had a 10% or greater decline in eGFR, 31.2% had a decline of 0% to 10%, 26.8% had an increase of 0% to 10%, and 16.8% had an increase greater than 10%.

There were associations between acute decline in eGFR and higher baseline urine albumin-to-creatinine ratio, eGFR, systolic BP, diuretic or beta-blocker use, and finerenone use. Overall, there were significant reductions in the composite cardiovascular and kidney outcomes. Results were similarly beneficial across eGFR subgroups. When modeled as a continuous variable, the risks for cardiovascular and kidney outcomes were reduced with finerenone use, irrespective of acute eGFR change (*P* interaction 0.58 and 0.36, respectively).

"The cardiovascular and kidney benefits of finerenone were not modified by an acute eGFR change after drug initiation," the researchers said.

DIALYSIS

Associations Between Sleep Patterns and Disorders in Patients on Hemodialysis

Kidney Med. doi:10.1016/j.xkme.2025.100976

Patients treated with hemodialysis commonly develop sleep disorders. However, there are few data available on the impact of sleep patterns on survival. To address the knowledge gap, **Yoko Narasaki, PhD, RD,** and colleagues conducted an observational cohort study designed to identify the presence and frequency of sleep disorders among patients receiving hemodialysis.

The researchers used data on patients treated with in-center hemodialysis from the multicenter prospective National Institutes of Health Malnutrition, Diet, and Racial Disparities in Chronic Kidney Disease cohort. Sleep patterns were identified using protocolized sleep surveys from March 2014 to June 2019. The outcome of interest in the current analysis was mortality.

The cohort included 452 participants. Mean age was 55 years, 46% were women, and median follow-up was 3.5 years. Results of expanded case-mix models suggested an association between shorter sleep duration (less than or equal to median of observed values) and higher mortality on dialysis (HR, 1.59; 95% CI, 1.09-2.31) and nondialysis (HR, 1.51; 95% CI, 1.04-2.19) days (ref: greater than median).

Mortality was higher among patients who reported high frequencies (often or almost always) of difficulty falling asleep (HR, 1.74; 95% CI, 1.17-2.58), feeling unrested (HR, 1.69; 95% CI, 1.1-2.5), fatigue/exhaustion after dialysis (HR, 2.42; 95% CI, 1.41-4.16), or fatigue/exhaustion on nondialysis days (HR, 1.73; 95% CI, 1.11-2.69) compared with patients who never or rarely reported having those symptoms.

There was an association between moderate to high frequency of sleeping pill use and higher mortality for sometimes and often/always use versus never/rare use of sleeping pills. There was also an association between patients reporting frequent apnea or restless leg syndrome and worse survival. There was no association between sleeping outside of the primary sleep period and worse survival.

In summary, the researchers said, "In a well-characterized prospective multicenter hemodialysis cohort, patients who reported shorter sleep duration, sleeping difficulty or feeling unrested, moderate to frequent sleeping pill consumption, and sleep disorders (sleep apnea and restless legs) had a higher mortality risk."

Pain-Associated Outcomes Improved With PCST

JAMA Intern Med. doi:10.1001/jamainternmed.2024.7140

Patients with dialysis-dependent kidney failure commonly develop chronic pain. **Laura M. Dember, MD,** and colleagues conducted a multicenter, randomized clinical trial designed to examine the effectiveness of pain coping skills training (PCST) compared with usual care. The study was held across 16 academic centers and 103 outpatient dialysis facilities in the US.

The study cohort included patients undergoing maintenance hemodialysis and experiencing chronic pain. Participants were randomly assigned 1:1 to PCST or usual care. Follow-up was 36 weeks. Enrollment began on January 4, 2021, and follow-up ended on December 21, 2023.

The study intervention included 12 weekly coach-led sessions via video or telephone conferencing, followed by 12 weeks of daily interactive voice response sessions. Patients in the usual care group received no trial-driven pain intervention. The Brief Pain Inventory (BPI) Interference subscale was used to measure the primary outcome of pain interference. Scores ranged from 0 to 10, with higher scores indicating more pain interference. Secondary outcomes were pain intensity, pain catastrophizing, quality of life, depression, and anxiety.

The overall cohort included 643 participants (PCST: n=319; usual care: n=324). Mean age was 60.3 years, and 44.8% of participants were female. At week 12, the reduction in the BPI Interference score was larger in the PCST group compared with the usual care group. The effect persisted at 24 weeks (between-group difference, –0.48; 95% CI –0.86 to –0.11). However, the effect was diminished at week 36.

At 24 weeks, a decrease in BPI Interference score greater than 1 point occurred in 55.9% of participants in the PCST group compared with 42.8% in the usual care group at 24 weeks. Changes for the secondary outcomes were favorable with PCST at week 36.

In summary, the authors said, "In this randomized clinical trial of patients undergoing maintenance hemodialysis, PCST had benefits on pain interference and other pain-associated outcomes. While the effect on the overall cohort was of modest magnitude, the intervention resulted in a clinically meaningful improvement in pain interference for a substantial proportion of participants."