ASN American Society of Nephrology

KIDNEY WEEK EDITION

KidneyNews

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How Might Eliminating Race-based Adjustments in Kidney Function Estimates Affect Kidney Transplant Waitlisting?

By Tracy Hampton

Recognizing that race is a social and not a biological construct, several health care institutions no longer report patients' kidney function through estimated glomerular filtration rate (eGFR) equations that have an adjustment for Black race. ASN and the National Kidney Foundation have endorsed this move, and a new set of race-free equations to estimate GFR was published in 2021.

New research published in *CJASN* (1) examines the impact of using these new equations on kidney transplant waitlist access.

The study looked specifically at how the new equations will affect when patients not yet treated with dialysis can begin to accrue wait time for transplantation—or preemptive waitlisting. eGFR is the primary criterion for determining eligibility for registration on the kidney transplant waitlist in these patients, and preemptive wait time accrual—or the waiting time that can accumulate before a patient starts dialysis—affects when a patient may ultimately receive an offer for a kidney transplant. According to current national policy, patients can begin to accrue wait time for transplantation when their eGFR is <20 mL/min/1.73 m^2.

Previously, the study's investigators showed that when using the older equation that included Black race, individuals of Black race had a shorter time to kidney failure (and would theoretically accrue less wait time). In the current research, the investigators wondered whether using new race-free equations to guide preemptive waitlisting would minimize racial differences in accruable preemptive wait time. The team determined the association between race (Black or White) and time spent with eGFR <20 mL/min/1.73 m^2 using the new race-free, creatinine-based equation or a new race-free, cystatin C-based equation.

When using the new race-free, creatinine-based equation, time to kidney failure was similar between patients of Black and White race; however, the time to kidney failure was still shorter for patients of Black race using the cystatin C-based, race-free equation.

The results suggest that using the race-free, creatinine-based equation to determine preemptive waitlist eligibility is the strategy that may reduce racial differences in access to preemptive wait time accrual.

"We believe that the findings in our study are helpful in providing some preliminary data on how use of the different GFR estimating equations would theoretically affect wait time accrual prior to the start of dialysis," said lead author Elaine Ku, MD, MAS, of the University of California, San

Continued on page 7 >

Kidney Week Scientific Sessions

THURSDAY

Preventing the Next Pandemic
Keynote Address: Peter J. Hotez, MD, PhD
Panel Moderator: Carlos del Rio, MD

Adeno-Associated Virus Genome Rescue of *NPHS2* in Mice
Michelle P. Winn, MD, Endowed Lectureship:
Moin Saleem, MBBS, MBChB, MD, PhD

Improving Kidney Graft Long-Term Outcomes: Lessons Learned and New Perspectives
Barbara T. Murphy, MB BAO BCh, FRCPI, Endowed Lectureship:
Roslyn B. Mannon, MD, FASN

Implementing Goal-Directed Medical Therapies for Diabetic Kidney Disease
Garabed Eknoyan, MD, Endowed Lectureship:
Katherine R. Tuttle, MD, FASN

Integrating Analysis of Animal Models and Human Biopsies to Better Understand AKI
Robert W. Schrier, MD, Endowed Lectureship:
Lloyd G. Cantley, MD, FASN

FRIDAY

Making the Impossible Possible: First-in-Human Clinical Grade Kidney Xenotransplant
State-of-the-Art Lecture: Jayme E. Locke, MD, MPH

Unexpected Roles for Renal Olfactory Receptors
ASN-AHA Donald W. Seldin Young Investigator Award:
Jennifer L. Pluznick, PhD

Fluid Management in Septic AKI: When, What Type, and How Much?
Burton D. Rose, MD, Endowed Lectureship:
Kathleen D. Liu, MD, PhD, FASN

Systems Biology Approach to Management of CKD-MBD
Jack W. Coburn, MD, Endowed Lectureship: Eleanor D. Lederer, MD, FASN

Incorporating Mental Health Practices by Increasing Psychosocial Education for Kidney Recipients
Celeste Castillo Lee Memorial Lectureship: Patrick O. Gee, Sr., PhD

SATURDAY

mRNA as Medicine
State-of-the-Art Lecture: Melissa J. Moore, PhD

Urea Transport to Nephrogenic Diabetes Insipidus: Using Physiology to Develop Novel Therapy
Homer W. Smith Award Lecture: Jeff M. Sands, MD, FASN

Developmentally Programming to a Healthy Kidney
Barry M. Brenner, MD, Endowed Lectureship:
Andrew P. McMahon, PhD, FRS

SUNDAY

Wearable Microfluidic Devices and Implantable Electronic Systems for Kidney Health
State-of-the-Art Lecture: John A. Rogers, PhD

Dialysis for Patients in the Undocumented Immigrant Community in the United States
Christopher R. Blagg, MD, Endowed Lectureship in Kidney Disease and Public Policy: Lilia Cervantes, MD

Inside

TAVNEOS®
(avacopan)

RELEASE

THE GRASP OF ANCA-ASSOCIATED VASCULITIS.

TAVNEOS® (avacopan) is a first-in-class, adjunctive treatment proven to help patients achieve and sustain remission.[1-4]

Discover more about TAVNEOS by scanning the QR code or visiting **TAVNEOS.com/hcp**

INDICATION

TAVNEOS is indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. TAVNEOS does not eliminate glucocorticoid use.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Serious hypersensitivity to avacopan or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hepatotoxicity: Serious cases of hepatic injury have been observed in patients taking TAVNEOS, including life-threatening events. Obtain liver test panel before initiating TAVNEOS, every 4 weeks after start of therapy for 6 months and as clinically indicated thereafter. Monitor patients closely for hepatic adverse reactions, and consider pausing or discontinuing treatment as clinically indicated (refer to section 5.1 of the Prescribing Information). TAVNEOS is not recommended for patients with active, untreated, and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis. Consider the risks and benefits before administering this drug to a patient with liver disease.

Serious Hypersensitivity Reactions: Cases of angioedema occurred in a clinical trial, including 1 serious event requiring hospitalization. Discontinue immediately if angioedema occurs and manage accordingly. TAVNEOS must not be readministered unless another cause has been established.

Hepatitis B Virus (HBV) Reactivation: Hepatitis B reactivation, including life-threatening hepatitis B, was observed in the clinical program. Screen patients for HBV. For patients with evidence of prior infection, consult with physicians with expertise in HBV and monitor during TAVNEOS therapy and for 6 months following. If patients develop HBV reactivation, immediately discontinue TAVNEOS and concomitant therapies associated with HBV reactivation, and consult with experts before resuming.

Serious Infections: Serious infections, including fatal infections, have been reported in patients receiving TAVNEOS. The most common serious infections reported in the TAVNEOS group were pneumonia and urinary tract infections. Avoid use of TAVNEOS in patients with active, serious infection, including localized infections. Consider the risks and benefits before initiating TAVNEOS in patients with chronic infection, at increased risk of infection, or who have been to places where certain infections are common.

ADVERSE REACTIONS

The most common adverse reactions (≥5% of patients and higher in the TAVNEOS group vs. prednisone group) were nausea, headache, hypertension, diarrhea, vomiting, rash, fatigue, upper abdominal pain, dizziness, blood creatinine increased, and paresthesia.

DRUG INTERACTIONS

Avoid coadministration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when coadministered with strong CYP3A4 enzyme inhibitors to 30 mg once daily. Monitor for adverse reactions and consider dose reduction of certain sensitive CYP3A4 substrates.

TAVNEOS is available as a 10 mg capsule.

Please see the Brief Summary of the Full Prescribing Information for TAVNEOS on the following pages.

To report a suspected adverse event, call 1-833-828-6367. You may report to the FDA directly by visiting www.fda.gov/medwatch or calling 1-800-332-1088.

References: 1. TAVNEOS® (avacopan) Prescribing Information. ChemoCentryx, Inc. **2**. Jayne DRW, Merkel PA, Schall TJ, Bekker P, for the ADVOCATE Study Group. Avacopan for the treatment of ANCA-associated vasculitis. *N Engl J Med*. 2021;384(7):599-609. doi:10.1056/NEJMoa2023386 **3**. Khan MM, Molony DA. In ANCA-associated vasculitis, avacopan was superior to prednisone taper for sustained remission. *Ann Intern Med*. 2021;174(7):JC79. doi:10.7326/ACPJ202107200-079 **4**. U.S. Food and Drug Administration. Novel drug approvals for 2021. Published November 2021. Accessed November 4, 2021. https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2021

CHEMOCENTRYX

TAVNEOS® (AVACOPAN) CAPSULES FOR ORAL USE BRIEF SUMMARY OF THE FULL PRESCRIBING INFORMATION (PI) — RX ONLY

INDICATIONS AND USAGE

TAVNEOS is indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. TAVNEOS does not eliminate glucocorticoid use.

DOSAGE AND ADMINISTRATION

Recommended Evaluations Prior to Treatment Initiation

Before initiating TAVNEOS, consider performing the following evaluations:

- Liver Function Tests: Obtain liver test panel (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin) before initiating TAVNEOS. TAVNEOS is not recommended for use in patients with cirrhosis, especially those with severe hepatic impairment (Child-Pugh C) *[see Warnings and Precautions (Full PI 5.1) and Use in Specific Populations (Full PI 8.7)]*.
- Hepatitis B (HBV) Serology: Screen patients for HBV infection by measuring HBsAg and anti-HBc. For patients with evidence of prior or current HBV infection, consult with a physician with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy before or during treatment with TAVNEOS *[see Warnings and Precautions (Full PI 5.3)]*.

Recommended Dosage and Administration

The recommended dose of TAVNEOS is 30 mg (three 10 mg capsules) twice daily, with food.

Advise patients that TAVNEOS capsules should not be crushed, chewed or opened.

If a dose is missed, instruct the patient to wait until the usual scheduled time to take the next regular dose. Instruct the patient not to double the next dose.

Dosage Modifications Due to CYP3A4 Inhibitors

Reduce the dosage of TAVNEOS to 30 mg once daily when used concomitantly with strong CYP3A4 inhibitors.

CONTRAINDICATIONS

TAVNEOS is contraindicated in patients with serious hypersensitivity reactions to avacopan or to any of the excipients *[see Warnings and Precautions (Full PI 5.2)]*.

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Serious cases of hepatic injury have been observed in patients taking TAVNEOS. During controlled trials, the TAVNEOS treatment group had a higher incidence of transaminase elevations and hepatobiliary events, including serious and life-threatening events *[see Adverse Reactions (Full PI 6.1)].*

Obtain liver test panel (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin) before initiating TAVNEOS, every 4 weeks after start of therapy for the first 6 months of treatment and as clinically indicated thereafter.

If a patient receiving treatment with TAVNEOS presents with an elevation in ALT or AST to >3 times the upper limit of normal, evaluate promptly and consider pausing treatment as clinically indicated.

If AST or ALT is >5 times the upper limit of normal, or if a patient develops transaminases >3 times the upper limit of normal with elevation of bilirubin to >2 times the upper limit of normal, discontinue TAVNEOS until TAVNEOS-induced liver injury is ruled out *[see Adverse Reactions (Full PI 6.1)]*.

TAVNEOS is not recommended for patients with active, untreated and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis. Consider the risk and benefit before administering this drug to a patient with liver disease. Monitor patients closely for hepatic adverse reactions *[see Use in Specific Populations (Full PI 8.7)]*.

Hypersensitivity Reactions

TAVNEOS may cause angioedema *[see Adverse Reactions (Full PI 6.1)]*. In clinical trials, two cases of angioedema occurred, including one serious event requiring hospitalization. If angioedema occurs, discontinue TAVNEOS immediately, provide appropriate therapy, and monitor for airway compromise. TAVNEOS must not be re-administered unless another cause has been established. Educate patients on recognizing the signs and symptoms of a hypersensitivity reaction and to seek immediate medical care should they develop.

Hepatitis B Virus (HBV) Reactivation

Hepatitis B virus (HBV) reactivation, including life threatening hepatitis B, was observed in the clinical program.

HBV reactivation is defined as an abrupt increase in HBV replication, manifesting as a rapid increase in serum HBV DNA levels or detection of HBsAg, in a person who was previously HBsAg negative and anti-HBc positive. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels. In severe cases, increase in bilirubin levels, liver failure, and death can occur.

Screen patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with TAVNEOS. For patients who show evidence of prior hepatitis B infection (HBsAg positive [regardless of antibody status] or HBsAg negative but anti-HBc positive), consult with physicians with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy before and/or during TAVNEOS treatment.

Monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis, or HBV reactivation during and for six months following TAVNEOS therapy. In patients who develop reactivation of HBV while on TAVNEOS, immediately discontinue TAVNEOS and any concomitant therapy associated with HBV reactivation, and institute appropriate treatment. Insufficient data exist regarding the safety of resuming TAVNEOS treatment in patients who develop HBV reactivation. Resumption of TAVNEOS treatment in patients whose HBV reactivation resolves should be discussed with physicians with expertise in managing HBV.

Serious Infections

Serious infections, including fatal infections, have been reported in patients receiving TAVNEOS. The most common serious infections reported in the TAVNEOS group were pneumonia and urinary tract infections.

Avoid use of TAVNEOS in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating TAVNEOS in patients:

- with chronic or recurrent infection
- who have been exposed to tuberculosis
- with a history of a serious or an opportunistic infection

- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or
- with underlying conditions that may predispose them to infection.

Closely monitor patients for the development of signs and symptoms of infection during and after treatment with TAVNEOS. Interrupt TAVNEOS if a patient develops a serious or opportunistic infection. A patient who develops a new infection during treatment with TAVNEOS should undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient; appropriate antimicrobial therapy should be initiated, the patient should be closely monitored, and TAVNEOS should be interrupted if the patient is not responding to antimicrobial therapy. TAVNEOS may be resumed once the infection is controlled.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:
- Hepatotoxicity *[see Warnings and Precautions (Full PI 5.1)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (Full PI 5.2)]*
- Hepatitis B Virus (HBV) Reactivation *[see Warnings and Precautions (Full PI 5.3)]*
- Serious Infections *[see Warnings and Precautions (Full PI 5.4)]*

Clinical Trials Experience

Because the clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The identification of potential adverse drug reactions was based on safety data from the phase 3 clinical trial in which 330 patients with ANCA-associated vasculitis were randomized 1:1 to either TAVNEOS or prednisone *[see Clinical Studies (Full PI 14)]*. The mean age of patients was 60.9 years (range of 13 to 88 years), with a predominance of men (56.4%) and Caucasians (84.2%). The cumulative exposure to TAVNEOS was 138.7 patient-years. Additionally, two phase 2 trials were conducted in ANCA-associated vasculitis. The cumulative clinical trial exposure from the phase 2 and 3 trials equals 212.3 patient-years.

The most frequent serious adverse reactions reported more frequently in patients treated with TAVNEOS than with prednisone were pneumonia (4.8% TAVNEOS vs. 3.7% prednisone), GPA (3.0% TAVNEOS vs. 0.6% prednisone), acute kidney injury (1.8% TAVNEOS vs. 0.6% prednisone), and urinary tract infection (1.8% TAVNEOS vs. 1.2% prednisone). Within 52 weeks, 4 patients in the prednisone treatment group (2.4%) and 2 patients in the TAVNEOS group (1.2%) died. There were no deaths in the phase 2 trials.

In the phase 3 trial, seven patients (4.2%) in the TAVNEOS treatment group and 2 patients (1.2%) in the prednisone treatment group discontinued treatment due to hepatic-related adverse reactions, including hepatobiliary adverse reactions and liver enzymes abnormalities. The most frequent adverse reaction that led to drug discontinuation reported by > 1 patient and more frequently reported in patients treated with TAVNEOS was hepatic function abnormal (1.8%).

The most common adverse reactions that occurred in ≥5% of patients and higher in the TAVNEOS group as compared with the prednisone group are listed in Table 1.

Table 1: Adverse Reactions Reported in ≥5% of Patients and Higher in TAVNEOS Group vs. Prednisone Group in Phase 3 Trial

Adverse Reaction	Prednisone (N=164) n (%)	TAVNEOS (N=166) n (%)
Nausea	34 (20.7)	39 (23.5)
Headache	23 (14.0)	34 (20.5)
Hypertension	29 (17.7)	30 (18.1)
Diarrhea	24 (14.6)	25 (15.1)
Vomiting	21 (12.8)	25 (15.1)
Rash	13 (7.9)	19 (11.4)
Fatigue	15 (9.1)	17 (10.2)
Upper abdominal pain	10 (6.1)	11 (6.6)
Dizziness	10 (6.1)	11 (6.6)
Blood creatinine increased	8 (4.9)	10 (6.0)
Paresthesia	7 (4.3)	9 (5.4)

N=number of patients randomized to treatment group in the Safety Population; n=number of patients in specified category.

Hepatotoxicity and Elevated Liver Function Tests

In the phase 3 trial, a total of 19 patients (11.6%) in the prednisone group and 22 patients (13.3%) in the TAVNEOS group had hepatic-related adverse reactions, including hepatobiliary adverse reactions and liver enzyme abnormalities. Study medication was paused or discontinued permanently due to hepatic-related adverse reactions in 5 patients (3.0%) in the prednisone group and 9 patients (5.4%) in the TAVNEOS group. Serious hepatic-related adverse reactions were reported in 6 patients (3.7%) in the prednisone group and 9 patients (5.4%) in the TAVNEOS group. A serious hepatic-related adverse reaction was reported in 1 patient in the TAVNEOS group in the phase 2 studies.

Angioedema

In the phase 3 trial, 2 patients (1.2%) in the TAVNEOS group had angioedema; one event was a serious adverse reaction requiring hospitalization.

Elevated Creatine Phosphokinase

In the phase 3 trial, 1 patient (0.6%) in the prednisone group and 6 patients (3.6%) in the TAVNEOS group had increased creatine phosphokinase. One TAVNEOS-treated patient discontinued treatment due to increased creatine phosphokinase.

DRUG INTERACTIONS

CYP3A4 Inducers

Avacopan exposure is decreased when co-administered with strong CYP3A4 enzyme inducers such as rifampin *[see Clinical Pharmacology (Full PI 12.3)]*. Avoid coadministration of strong and moderate CYP3A4 inducers with TAVNEOS.

CYP3A4 Inhibitors

Avacopan exposure is increased when co-administered with strong CYP3A4 enzyme inhibitors such as itraconazole *[see Clinical Pharmacology (Full PI 12.3)]*. Administer TAVNEOS 30 mg once daily when coadministered with strong CYP3A4 inhibitors.

CYP3A4 Substrates

Avacopan is a CYP3A4 inhibitor. Closely monitor patients for adverse reactions and consider dose reduction of sensitive CYP3A4 substrates with a narrow therapeutic window when coadministered with TAVNEOS *[see Clinical Pharmacology (Full PI 12.3)]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate and well-controlled studies with TAVNEOS in pregnant women to inform a drug-associated risk. In animal reproduction studies, oral administration of avacopan to pregnant hamsters and rabbits during the period of organogenesis produced no evidence of fetal harm with exposures up to approximately 5 and 0.6 times, respectively, the exposure at the maximum recommended human dose (MRHD) of 30 mg twice daily (on an area under the curve [AUC] basis). Avacopan caused an increase in the number of abortions in rabbits at an exposure 0.6 times the MRHD *(see Animal Data)*. The background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In an embryo-fetal development study with pregnant hamsters dosed by the oral route during the period of organogenesis from gestation days 6 to 12, avacopan produced an increase in the incidence of a skeletal variation, described as supernumerary ribs, at an exposure that was 5 times the MRHD (on an AUC basis with a maternal oral dose of 1000 mg/kg/day). No structural abnormalities were noted with exposures up to 5 times the MRHD (on an AUC basis with maternal oral doses up to 1000 mg/kg/day).

In an embryo-fetal development study with pregnant rabbits dosed by the oral route during the period of organogenesis from gestation days 6 to 18, avacopan caused an increase in the number of abortions at an exposure 0.6 times the MRHD (on an AUC basis with a maternal oral dose of 200 mg/kg/day), however, no evidence of fetal harm was observed with such exposures. Maternal toxicity, as evidenced by decreased body weight gains, was observed at exposures 0.6 times and higher than the MRHD (on an AUC basis with maternal oral doses of 30 mg/kg/day and higher).

In a prenatal and postnatal development study with pregnant hamsters dosed by the oral route during the periods of gestation and lactation from gestation day 6 to lactation day 20, avacopan had no effects on the growth and development of offspring with exposures up to approximately 5 times the MRHD (on an AUC basis with maternal oral doses up to 1000 mg/kg/day).

Lactation

Risk Summary

There are no available data on the effects of avacopan on the breastfed child or on milk production. It is unknown whether avacopan is secreted in human milk. Avacopan was detected in the plasma of undosed hamster pups nursing from drug-treated dams *(see Animal Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TAVNEOS and any potential adverse effects on the breast-fed infant from TAVNEOS or from the underlying maternal condition.

Animal Data

Avacopan has not been measured in the milk of lactating animals; however, it was detected in the plasma of nursing offspring in a pre- and post-natal development study with hamsters at a pup to maternal plasma ratio of 0.37. This finding suggests that avacopan is secreted into the milk of lactating hamsters *[see Nonclinical Pharmacology (Full PI 13.1)]*.

Pediatric Use

The safety and effectiveness of TAVNEOS in pediatric patients have not been established.

Geriatric Use

Of the 86 geriatric patients who received TAVNEOS in the phase 3 randomized clinical trial for ANCA-associated vasculitis *[see Clinical Studies (Full PI 14)]*, 62 patients were between 65-74 years and 24 were 75 years or older. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients.

Patients With Renal Impairment

No dose adjustment is required for patients with mild, moderate, or severe renal impairment *[see Clinical Pharmacology (Full PI 12.3)]*. TAVNEOS has not been studied in patients with ANCA-associated vasculitis who are on dialysis.

Patients With Hepatic Impairment

No dosage adjustment is recommended for patients with mild or moderate (as indicated by the Child-Pugh method) hepatic impairment *[see Clinical Pharmacology (Full PI 12.3)]*. TAVNEOS has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

Based on Prescribing Information approved on 10/2021.

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KidneyNews

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Eliminating Race-based Adjustments

Continued from cover

Francisco. "We found that the new creatinine-based equation seemed to be associated with more similar wait time that could potentially be accrued compared with use of the cystatin C-based equation, but our findings require further validation in larger groups of patients."

An accompanying editorial by Rhiannon D. Reed, DrPH, and Jayme E. Locke, MD, MPH, FACS, FAST (2), both of the University of Alabama at Birmingham, notes that although a race-free, creatinine-based equation for eGFR may attenuate racial differences in access to kidney transplantation, it is uncertain what consequences there may be from widespread implementation of this formula.

. . . [I]t is uncertain what consequences there may be from widespread implementation of this formula.

"While the number of Blacks affected by use of the new formula will be smallest for dialysis initiation and referral for transplantation, more Blacks will be affected at higher eGFR thresholds, including kidney donor candidacy and post-donation follow-up. There would be a corresponding increase in the prevalence of chronic kidney disease among individuals in the general population who identify as Black and may now be excluded from kidney donation, thus limiting access to living donation in a population already at a disadvantage," the authors wrote. "There are also potential implications for enrollment and conduct of clinical trials, such as fewer outcomes observed in trials where events are more likely to occur in those with lower eGFR who may now be excluded. Furthermore, while systematic overestimation among non-Blacks has the potential to result in inappropriate drug continuation or overdosing for medications, underestimation among Blacks may result in drug discontinuation and underdosing, including chemotherapeutic agents and weight loss medications." ■

References

1. Ku E, et al. Comparison of 2021 CKD-EPI equations for estimating racial differences in preemptive waitlisting for kidney transplantation. *Clin J Am Soc Nephrol*, published online ahead of print September 19, 2022. doi: 10.2215/CJN.04850422; https://cjasn.asnjournals.org/content/early/2022/09/19/CJN.04850422?with-ds=yes

2. Reed RD, Locke JE. Reducing racial disparities in access to transplant in the United States. One step at a time. *Clin J Am Soc Nephrol*, published online ahead of print September 19, 2022. doi: 10.2215/CJN.09590822; https://cjasn.asnjournals.org/content/early/2022/09/19/CJN.09590822

Apply Now to Be a *KN* Editorial Fellow

ASN *Kidney News*—the kidney community's leading newsmagazine—invites you to become a *KN* Editorial Fellow.

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Two fellows will be selected for the program. They will work closely with an assigned mentor and the Editor-in-Chief.

What's the deadline to apply? October 30, 2022.
When does the program begin? The fellowship begins January 1, 2023.
How do I apply? Apply at https://www.asn-online.org/knfp and provide the following:

- A brief bio
- A detailed CV
- A commitment and recommendation letter from Division Chief or Program Director of fellowship specifying how you are suited for the position
- A 200- to 300-word short article on the topic, "Training in Nephrology 2023: What can be changed?" One original figure and/or a visual abstract may be included. No co-authors are allowed.

ASN Kidney News *embraces diversity and equal opportunity. We are committed to building an inclusive culture that represents the diverse backgrounds, perspectives, and skills of the communities we serve globally.*

ASN Executive Vice President's Update

ASN Kidney Week 2022: What's New, Exciting, and Innovative?

By Tod Ibrahim

Kidney Week is central to ASN's long tradition of supporting undergraduate, graduate, and continuing education. Each year, Kidney Week brings together members of the kidney community from more than 120 countries: scientists to clinicians, medical students to emeritus professors, startups to well-established companies, and first-time participants to a few people who have attended every meeting since 1967.

For 2022, Kidney Week includes Early Programs and the ASN Annual Meeting:

- Four fully virtual Early Programs will be live streamed on Wednesday, October 26, and Thursday, October 27.
- Three Early Programs will be held in-person on Wednesday, November 2.
- The Annual Meeting will take place Thursday, November 3, through Sunday, November 6.

What's new this year?

Building on the success of last year, ASN and the National Academy of Medicine (NAM) have organized the opening plenary session on Thursday, November 3, featuring an expert panel on "Preventing the Next Pandemic" (Table 1). The other three plenary sessions will feature state-of-the-art lectures by Jayme E. Locke, MD, MPH (Friday, November 4), Melissa J. Moore, PhD (Saturday, November 5), and John A. Rogers, PhD (Sunday, November 6).

At this year's meeting, ASN will twice recognize Barbara T. Murphy, MB BAO BCh, FRCPI. The Barbara T. Murphy Award honors leaders who strengthen the foundation of nephrology while advancing the field through innovation, creativity, inspiration, and tenacity and have the courage to forge new paths, overcome challenges, and serve as exemplars for future generations of nephrologists to admire, emulate, and amplify. This award was launched last year with Dr. Murphy as the inaugural recipient. This year's recipient is Julie R. Ingelfinger, MD, a deputy editor for *The New England Journal of Medicine*, professor of pediatrics at Harvard Medical School, and consulting pediatric nephrologist at Massachusetts General Hospital.

Additionally, ASN is pleased to announce a new endowed lecture honoring Dr. Murphy's leadership in transplant immunology and medicine. Roslyn B. Mannon, MD, FASN, will deliver the inaugural lecture on "Improving Kidney Graft Long-Term Outcomes: Lessons Learned and New Perspectives." A former President of the American Society of Transplantation (AST), the current Chair of the ASN Policy and Advocacy Committee, and a current member of the ASN Grants Review Committee, Dr. Mannon is a professor of medicine, pathology, and microbiology at the University of Nebraska Medical Center; vice chair for academic development and research mentoring; and associate chief of nephrology for research. ASN gratefully acknowledges Verici Dx, Renalytix, and AST for supporting this new lecture.

As part of its commitment to include the patient voice throughout the organization and across its activities, ASN is launching "Cele's Champions: Cele Fogarty Travel Support Program for Patients" at this year's meeting. In honor of former ASN Vice President of Meetings and Member Experience Cecilia "Cele" Agnes Fogarty—who worked every ASN Annual Meeting/Renal Week/Kidney Week from 1988 through 2020—ASN is providing travel support to 10 people with kidney diseases or their care partners to attend Kidney Week.

This year's meeting will include three new Early Programs ("Advances in Research Conference: Regenerative Medicine and Bioartificial Kidneys," "Point-of-Care Ultrasound in Nephrology," and "Renal Physiology: Structure and Function in Kidney Health and Disease"). Recurring from previous meetings, the other Early Programs are "Critical Care Nephrology: 2022 Update," "Fundamentals of Renal Pathology," "Glomerular Diseases: 2022 Update," and "Maintenance Dialysis." For the first time ever, three of these programs will be in person, and four will be held fully virtually.

What's exciting scientifically and clinically?

"After three long years, I'm beyond thrilled we will be able to meet in person," said ASN President Susan E. Quaggin, MD, FASN. "And of the several thousand Kidney Week participants, we will welcome more than 775 faculty and presenters as well as over 400 recipients of travel support from ASN, mostly medical students, graduate students, residents, and fellows, and now patients." The infographic illustrates ASN Kidney Week 2022 by the numbers.

"This year's meeting highlights how the nephrology community has adapted and developed cutting-edge technologies through the challenges of the past few years, as highlighted in our program from plenaries to poster presentations," emphasized ASN Kidney Week Education Committee Cochair Catherine Godson, PhD. "It is fantastic that we have the opportunity to develop and reinvigorate collaborative and social networks through Kidney Week."

Her fellow cochair, Kirk N. Campbell, MD, FASN, added, "Attendees can expect a dynamic program featuring advances ranging from enhanced understanding of the molecular architecture of the human kidney to novel therapeutic interventions and implementation science, a continuum grounded in the central mission of improving outcomes in patients living with kidney diseases."

This year's "High-Impact Clinical Trials"—taking place on Friday, November 4, from 10:30 a.m. to 12:30 p.m. EDT—promises exciting breakthroughs that will generate excitement in the convention center and throughout the world. The session highlights randomized trials (Phase II and III) that will have significant impact on clinical practice.

To improve patient care, ASN is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC) to provide continuing education for the health care team. Physicians, nurses, pharmacists, and physician assistants can claim a maximum of 75 continuing education credit hours for participating in the Annual Meeting during Kidney Week 2022. Please note that Early Programs also offer continuing education credits that vary by participating program.

Additionally, diplomates of either the American Board of Internal Medicine or the American Board of Pediatrics (ABP) can claim up to 75 maintenance of certification (MOC) points for participating in the Annual Meeting. This is the first year that ABP MOC points will be offered for the Annual Meeting.

What's innovative about the in-person and virtual options?

Given the desire of many in the kidney community for in-person networking, engagement, and interactivity, this year's Kidney Week includes in-person and virtual options for all participants. This is the first in-person Kidney Week since November 2019, or 1089 days since the community said their goodbyes in Washington, DC.

Those who participate in person will enjoy real-time sessions, events, and interactions; networking; and the scientific exposition, which includes the poster and exhibit halls. In addition to the ASN Welcome Reception, the meeting will include:

- Annual Wesson-Himmelfarb Diversity and Inclusion Lunch that aims to connect diverse members of the ASN community and foster dialogue with the ASN Council and other leaders in the field around ongoing diversity, equity, inclusion, and justice initiatives.
- LGBTQ+ and Allies Member Reception.

The participants who choose the virtual option will enjoy lower registration fees, the convenience of not traveling, and the ability to access content from anywhere. These participants can also live stream the four plenary sessions, the late-breakers, and several other sessions.

All meeting content will be available on the virtual meeting platform for in-person and virtual participants through Wednesday, December 21, 2022. In mid-January 2023, this content will move to the ASN eLearning Center for up to three 3 years and continue to be complimentary to meeting participants who obtain an access code. ■

Table 1. ASN-NAM Panel on Preventing the Next Pandemic

Speaker	Institution
Carlos del Rio, MD, Moderator	Emory University
Timothy G. Evans, MD, PhD, Panelist	McGill University
Peter J. Hotez, MD, PhD, Keynote	Baylor College of Medicine
Jennifer B. Nuzzo, DrPH, Panelist	Brown University School of Public Health
Reed V. Tuckson, MD, Panelist	Tuckson Health Connections

Tod Ibrahim, MLA, is Executive Vice President, American Society of Nephrology, Washington, DC.

Acknowledgment: Mr. Ibrahim thanks ASN Vice President of Kidney Week and Meetings Jin Soo Kim for her help with this editorial.

10,000

Participants, including every member of the kidney care, research, and education teams

3,000

Posters covering a wide variety of nephrology topics and perspectives, including basic, clinical, and translational science, as well as epidemiology and public health research

775

Faculty and oral abstract presenters

400

Recipients of travel support funding, including ASN Kidney STARS (students and residents); Karen L. Campbell, PhD, Fellows; William E. Mitch, III, MD, FASN, International Scholars; Cele's Champions; and Advances in Research Conference Early Program

300

Ancillary events sponsored by other members of the kidney community, such as Women in Nephrology

140

Companies and other members of the kidney community participating in the ASN Scientific Exposition on Thursday, November 3; Friday, November 4; and Saturday, November 5

16

Learning pathways, including "Acute Kidney Injury and Critical Care," "Fluid, Electrolyte, and Acid-Base Disorders," and "Kidney Transplantation"

12

Exhibitor Spotlights that highlight the most recent advances in nephrology practices, products, services, and technologies

11

Educational Symposia

KIDNEY WEEK 2022

Educational Symposia SCHEDULE

Thursday, November 3 – Saturday, November 5
12:45-1:45 p.m. Daily | Hyatt Regency Orlando

Lunch will be served at each symposium.

Seating is limited and available on a first-come, first-served basis to fully paid Annual Meeting participants. Doors open approximately 15 minutes prior to each symposium.

Continuing Education Credit

This live activity is eligible for continuing education credit. Please visit www.asn-online.org/kidneyweek for more information.

Thursday, November 3

Hope in ADPKD: Innovation in Therapeutics
Support is provided by an educational grant from ***Otsuka America Pharmaceutical, Inc.***

IgA Nephropathy: The Role of the Renal Endothelin System and Other Therapeutic Implications
Support is provided by an educational grant from ***Travere Therapeutics, Inc.***

Management of Hyperphosphatemia in Patients with ESKD, Especially During the COVID-19 Pandemic
Support is provided by an educational grant from ***Fresenius Medical Care Renal Therapies Group.***

Updates on Therapeutic Options for Anemia in Kidney Diseases
Support is provided by an educational grant from ***GlaxoSmithKline.***

Friday, November 4

Complement in IgA Nephropathy and Lupus Nephritis: Role in Pathogenesis and Implications for Treatment
Support is provided by an educational grant from ***Alexion Pharmaceuticals, Inc.***

Current and Future Approaches to the Diagnostic Assessment and Management of AKI in Patients with Cirrhosis
Support is provided by an educational grant from ***Mallinckrodt Pharmaceuticals.***

Hyperphosphatemia Management in Adults Treated with Dialysis for Kidney Failure: Old Lessons, New Directions
Support is provided by an educational grant from ***Akebia Therapeutics, Inc.***

Update on the Management of Recurrent Hyperkalemia Associated with RAAS Inhibitors in Patients with CKD and ESRD
Support is provided by an educational grant from ***CSL Vifor.***

Saturday, November 5

Emerging Therapies for ANCA-Associated Vasculitis
Support is provided by an educational grant from ***ChemoCentryx, Inc.***

Hyperkalemia: Understanding and Applying Innovative Approaches to the Management of CKD and ESKD
Support is provided by an educational grant from ***AstraZeneca Pharmaceuticals.***

Recognizing and Managing the Itch of CKD-Associated Pruritus: Scratching the Surface
Support is provided by an educational grant from ***CSL Vifor.***

All in-person symposia will be recorded and available in the meeting virtual platform through December 21. In mid-January, this content will be available in the ASN eLearning Center for up to three years; continuing education credits will not be awarded for the online content viewed after December 21.

ASN
American Society of Nephrology

KIDNEY MEDICINE IS A TEAM SPORT

Physician Assistants in Nephrology: Training, Pathway, and Scope

By Sara Krome

Physician assistants (PAs) have been colleague providers in health care since the late 1960s (1). PAs are trained at accredited PA programs across the country in the "medical" model of instruction, in contrast to nurse practitioners trained by the nursing instruction model (2). Most PA programs offer graduate-level education, with a degree such as Master of Health Science or Master of Physician Assistant Studies. A few programs remain that offer PA degrees or certificates at the baccalaureate level. Most graduate programs are 27 months (3). PAs are not required to and do not routinely complete a post-graduate residency, although there are some 1-year residencies offered in fields such as cardiology, critical care, cardiothoracic surgery, and hematology or oncology (4), although not in nephrology (3). Most PAs are required to be board certified. (An exception is with the Department of Veterans Affairs, in which PAs can be licensed and/or certified.) The certification is offered in internal medicine, general surgery, or family practice. Even PAs in specialty care are required to have certification in one of the above fields to practice.

PA certification lasting 10 years requires passing a certification exam and 100 hours of continuing medical education (CME; at least 50 hours must be category 1) completed every 2 years with an accompanying fee.

For PAs interested in a career in nephrology, they can begin by exploring nephrology in their elective rotations during PA student instruction. Some graduates enter nephrology upon graduation from their PA program; others elect to pursue working for a period of time in an internal medicine field to hone their clinical skills.

After at least 1 year in nephrology practice, the PA can consider pursuing a certificate of expertise in nephrology, called the Certificate of Added Qualifications. This is pursued through the PA-certifying body, the National Commission on Certification of Physician Assistants. Candidates must meet the following requirements: current PA certification, license for unrestricted practice in their state (or unrestricted privileges at a government agency), 2 years' experience (1 year of which must be nephrology), 75 hours of category 1 nephrology CME (25 hours of which must be obtained 2 years before the exam date), attestation from a colleague, and passing a nephrology specialty exam (5).

PAs in nephrology work in all areas, including inpatient nephrology manage-

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Physician Assistants in Nephrology

Continued from page 11

ment and coverage, outpatient clinic general nephrology (chronic kidney disease and transplant), dialysis care, home therapy, and even taking calls. Although PAs are dependent providers, much of their work is autonomous with highly effective relationships with their collaborating physician partners. PAs have prescriptive privileges in all 50 states, and many PAs perform procedures such as line placement (temporary dialysis catheters and central line placements) and percutaneous biopsies (including the kidney) (6).

A career as a nephrology PA is rewarding, and many different models of incorporation exist. As the nephrology workforce continues to expand, and more PAs join nephrology groups, it is important to know the educational pathway of this unique group of health care providers. There is also an important opportunity to develop unique resources to enrich educational opportunities. ■

Sara Krome, PA-C, is with the Durham VA Health Care System, Nephrology, Durham, NC.

Ms. Krome, PA-C, graduated from Duke University in 1992 with a Master of Health Science and has been a PA for 30 years. She entered the field of nephrology 16 years ago and works at the Durham VA Health Care System, which is affiliated with Duke University. Her primary practice is in the outpatient setting of general nephrology and peritoneal dialysis. She works with a group of 15 physicians and five advanced practice providers.

The author reports no conflicts of interest.

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Two More Studies Show Nova POC Creatinine/eGFR is As Accurate or More Accurate Than Laboratory Methods

Study One:

Accuracy Equal to Traceable Gold Standard Creatinine Method

Nova StatSensor capillary and venous whole blood POC specimens were directly compared to the same patient's venous samples measured by the laboratory gold standard ID-LCMS creatinine method. StatSensor POC concordance with ID-LCMS at a creatinine decision-making level of 1.2 mg/dL performed equally to the laboratory.

"Consequently, the sensitivity and specificity of the capillary blood testing post-calibration alignment was 100% and 98.3% respectively, indicating that the device is suitable to screen for CKD in POC settings and is a reliable method to assess a patient's renal status in the field."

Dubois JA et al. Creatinine standardization: a key consideration in evaluating whole blood creatinine monitoring systems for CKD screening. Analytical and Bioanalytical Chemistry (2022) 414:3279–3289.

Study Two:

Accuracy Better Than the Laboratory Jaffe Creatinine/eGFR Method

StatSensor Creatinine/eGFR showed better accuracy than the Jaffe creatinine/eGFR at identifying patients in the decision-making eGFR range of 60-89 when both methods were compared to the gold standard measured GFR.

"The performance of POC devices [StatSensor] to detect eGFR in the range 60–89 mL/min/1.73 m2 is of particular interest. With limited access to renal replacement therapy for severe kidney disease, it is advantageous to detect individuals with early disease who may benefit from renal protective measures. There was improved accuracy in this area compared to laboratory Jaffe measurements."

Currin S et al. Evaluating chronic kidney disease in rural South Africa: comparing estimated glomerular filtration rate using point-of-care creatinine to iohexol measured GFR. Clin Chem Med Lab 2021

StatSensor®

Point-of-Care Whole Blood Creatinine and eGFR Testing

nova® biomedical

novabiomedical.com

Reconsidering the Future of Nephrology and Reimagining Nephrology Fellowship Training

By Melissa West

In March, the ASN Council responded to requests from the Accreditation Council for Graduate Medical Education (ACGME) and the American Board of Internal Medicine (ABIM) to provide feedback on what changes should be made to nephrology certification and recertification (by ABIM) and fellowship training program requirements (by ACGME). Rather than taking a narrow view on procedural or program requirements, the ASN Council established the ASN Task Force on the Future of Nephrology to reconsider all aspects of the future of nephrology and develop recommendations for how to best prepare nephrology fellows for the challenges and opportunities the future will bring. The task force is made up of a diverse cross-section of ASN members (see box). "Nephrology is a vital and rewarding specialty, but every profession evolves and changes over time. I was drawn to serve on the task force because I wanted to contribute to thinking about and planning for where our field is headed in the future," shared Benjamin D. Humphreys, MD, PhD, FASN, a member of the ASN Task Force on the Future of Nephrology.

It *is* an exciting time for kidney care. Developments include the availability and use of big data, new payment models and value-based care, precision medicine, innovative therapies and devices, and a shifting perspective to protecting kidney health rather than managing kidney failure. These developments and others provide new career opportunities and considerations for the kidney care team. With the changing health care landscape, along with the ongoing evolution in kidney care, this year has provided an opportunity to reflect on the future of nephrology.

"I feel like we're on the cusp of many exciting advances in nephrology—from work done to delay or prevent diabetic nephropathy [and] new home dialysis equipment/opportunities to give patients more freedom to the exciting work of xenotransplantation and/or an artificial kidney," said Janis M. Orlowski, MD, ASN Task Force member. "This is an exciting time to be a nephrologist."

Since April when the task force was established, many key stakeholders have had an opportunity to share their perspective on the future of nephrology, including training and certification. Through a series of listening sessions and written requests, the task force has digested and deliberated the perspectives of many diverse stakeholders, as well as reviewed data collected from fellows, ABIM diplomates, training program directors, and the ASN Data Resource Center's effort to better understand the workforce. Task force member Joshua S. Waitzman, MD, PhD, said, "The power of data has been striking. By understanding the current practice patterns of today's nephrologists, I think we can make more workable procedure requirements. By surveying our current fellows

ASN Task Force on the Future of Nephrology

Sharon Anderson, MD, FASN, Oregon Health and Science University

Samira S. Farouk, MD, MS, FASN, Icahn School of Medicine at Mt. Sinai

Keisha L. Gibson, MD, FASN, MPH, ASN Council Liaison, University of North Carolina, Chapel Hill

Robert S. Hoover, Jr., MD, FASN, Tulane University School of Medicine

Benjamin D. Humphreys, MD, PhD, FASN, Washington University School of Medicine

Janis M. Orlowski, MD, Association of American Medical Colleges (former)

Mark E. Rosenberg, MD, FASN, Chair, University of Minnesota Medical School

Suneel M. Udani, MD, FASN, Nephrology Associates of Northern Illinois and Indiana

Joshua S. Waitzman, MD, PhD, Beth Israel Deaconess Medical Center

and younger attendings, we have a clear sense of what clinical needs they see and what additional training would be helpful to a next generation of nephrologists."

The final draft report of the task force will be released in late October, and the recommendations will be discussed at a special ASN Kidney Week event entitled, "Reimagining Nephrology Fellowship Training: Recommendations from the 2022 ASN Task Force on the Future of Nephrology," to be held on Thursday, November 3, from 10:30 a.m. to 12:00 p.m. in the Orlando Convention Center. Members of the task force will review the recommendations, including the rationale and potential next steps, followed by questions and discussion from attendees. "If the task force could accomplish one objective, I would prioritize enhancing and optimizing training opportunities for nephrology fellows, so they are educated and well-equipped to deliver high-quality, personalized treatment options for patients with advanced kidney disease, including home dialysis modalities, kidney transplantation, or conservative care," suggested Samira S. Farouk, MD, MS, FASN, task force member.

"It has been an honor to serve ASN as the chair of this task force and to work with such highly engaged task force members and ASN staff. I have always felt a strong passion and commitment for nephrology fellowship education and feel this is the time to reimagine how to best prepare our fellows for future practice as well as to increase the attractiveness of our field. I hope ASN members find our final report to be invigorating and refreshing," said Mark E. Rosenberg, MD, FASN. "Join us in Orlando for this special event—we want to hear from you."

Dialysis Center Ownership Affects Time to Transplant in Children

Among pediatric patients with end stage kidney disease (ESKD), as with adults, those receiving care at for-profit dialysis facilities have longer times to waitlisting and kidney transplantation, reports a study in the *Journal of the American Medical Association*.

The researchers analyzed data from the US Renal Data System on 13,333 pediatric patients (younger than 18 years) who initiated dialysis at US facilities between 2000 and 2018, with follow-up through 2019. The patients were 55% male and 45% female, and median age was 12 years. Twenty-eight percent were Hispanic, and 25% were non-Hispanic Black. At follow-up, time to kidney transplant waitlisting and transplant receipt were compared for patients receiving care at for-profit versus nonprofit dialysis facilities.

The analysis included 3618 patients receiving dialysis at for-profit centers, 7907 at nonprofit centers, and 1748 who switched from one type of center to the other. Patients receiving care at for-profit facilities were older: median age, 13 versus 10 years. Rural patients were more likely to be treated at for-profit centers, whereas patients in the Northeast region were more likely to receive care at nonprofit facilities.

Overall, 76% of patients were placed on the transplant waitlist during follow-up. At a median follow-up of 0.87 years, incidence of waitlisting was 36.2 per 100 person-years at for-profit facilities versus 49.8 per 100 person-years at nonprofit facilities. The adjusted hazard ratio for waitlisting at for-profit dialysis centers was 0.79.

At a median follow-up of 1.52 years, 69% of patients received a kidney transplant. Rates of kidney transplantation were lower for young patients treated at for-profit dialysis centers: 21.5 versus 31.3 per 100 person-years, and the adjusted hazard ratio was 0.71.

Previous studies have reported lower transplantation and survival rates for adult ESKD patients receiving care

at for-profit dialysis centers. The new study finds lower rates of waitlisting and transplant receipt for children and adolescents treated at for-profit versus nonprofit facilities.

The study "raises concerns that pediatric patients with ESKD may be disadvantaged for transplant access when they receive care at profit facilities," the researchers wrote. They discussed their findings in light of ongoing efforts to ensure access to transplantation for children with ESKD [Amaral S, et al. Association between dialysis facility ownership and access to the waiting list and transplant in pediatric patients with end-stage kidney disease in the US. *JAMA* 2022; 328:451–459. doi: 10.1001/jama.2022.11231].

Subclinical Inflammation Increases Long-Term Rejection and Graft Loss

Markers of subclinical inflammation detected on surveillance kidney allograft biopsies are associated with elevated long-term risk of rejection and graft loss, reports a preproof paper in *Kidney International*.

From a cohort of 1000 sequential kidney transplant recipients at the authors' center from 2013 to 2017, the analysis included 586 patients who underwent surveillance biopsy in the first year after transplantation and did not experience clinical rejection. Of these, 304 patients were found to have subclinical inflammation with tubulitis (SCI-T). This group was further classified as having subclinical borderline changes (182 patients) or subclinical T-cell-mediated rejection (122 patients; based on a Banff 2019 classification of 1A or higher.).

Over a median follow-up of 5 years, clinical and immunologic events were analyzed in terms of the presence and type of subclinical inflammation. The primary outcomes were clinical biopsy-proven acute rejection (C-BPAR) after the index biopsy and death-censored graft loss.

Episodes of C-BPAR were observed at a median follow-up of 2 years. This outcome was significantly more

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Subclinical Inflammation

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frequent in the combined SCI-T group compared with patients with no subclinical inflammation (17% vs. 4.6%; adjusted odds ratio [OR], 3.8). Patients with SCI-T were also at higher risk for death-censored graft loss (OR, 1.99). Alloimmune injury was more likely to be the cause of graft loss in the SCI-T group (67% vs. 50%).

Previous studies have suggested that low-level inflammation early after transplantation may be associated with an increased risk of adverse outcomes. However, there are few data on how subclinical inflammation on surveillance biopsies affects long-term allograft survival.

This 5-year follow-up study shows increased risks of C-BPAR and death-censored graft loss in kidney transplant recipients. Early surveillance biopsies may identify patients at higher risk for poor long-term outcomes, potentially enabling more personalized approaches to immunosuppression. The researchers note, "[T]he prognosis of SCI-T in general is good if not followed by subsequent clinical rejection" [Mehta RB, et al. Long-term immunological outcomes of early subclinical inflammation on surveillance kidney allograft biopsies. *Kidney Int*, published online ahead of print August 29, 2022. doi: 10.1016/j.kint.2022.07.030; https://www.kidney-international.org/article/S0085-2538(22)00686-X/fulltext]. ■

New Models Predict AKI Outcomes in ICU Patients

A pair of clinical models developed using machine learning techniques perform well in predicting the risk of death and adverse kidney outcomes in critically ill patients with incident acute kidney injury (AKI), reports a pre-proof paper in the *American Journal of Kidney Diseases*.

The multicenter, retrospective cohort study included a derivation set of 7354 patients at one U.S. university medical center who were diagnosed with AKI (based on serum creatinine Kidney Disease: Improving Global Outcomes [KDIGO] criteria) within 3 days after intensive care unit (ICU) admission. Data on 71 validated clinical

Table 2: Incidence of Overall[a] and Severe[b] Hypoglycemic Events in Placebo-Controlled Clinical Studies[c]

Monotherapy (24 weeks)	**Placebo (n=229)**	**JARDIANCE 10 mg (n=224)**	**JARDIANCE 25 mg (n=223)**
Overall (%)	0.4	0.4	0.4
Severe (%)	0	0	0
In Combination with Metformin (24 weeks)	**Placebo + Metformin (n=206)**	**JARDIANCE 10 mg + Metformin (n=217)**	**JARDIANCE 25 mg + Metformin (n=214)**
Overall (%)	0.5	1.8	1.4
Severe (%)	0	0	0
In Combination with Metformin + Sulfonylurea (24 weeks)	**Placebo (n=225)**	**JARDIANCE 10 mg + Metformin + Sulfonylurea (n=224)**	**JARDIANCE 25 mg + Metformin + Sulfonylurea (n=217)**
Overall (%)	8.4	16.1	11.5
Severe (%)	0	0	0
In Combination with Pioglitazone +/- Metformin (24 weeks)	**Placebo (n=165)**	**JARDIANCE 10 mg + Pioglitazone +/- Metformin (n=165)**	**JARDIANCE 25 mg + Pioglitazone +/- Metformin (n=168)**
Overall (%)	1.8	1.2	2.4
Severe (%)	0	0	0
In Combination with Basal Insulin +/- Metformin (18 weeks[d])	**Placebo (n=170)**	**JARDIANCE 10 mg (n=169)**	**JARDIANCE 25 mg (n=155)**
Overall (%)	20.6	19.5	28.4
Severe (%)	0	0	1.3
In Combination with MDI Insulin +/- Metformin (18 weeks[d])	**Placebo (n=188)**	**JARDIANCE 10 mg (n=186)**	**JARDIANCE 25 mg (n=189)**
Overall (%)	37.2	39.8	41.3
Severe (%)	0.5	0.5	0.5

[a]Overall hypoglycemic events: plasma or capillary glucose of less than or equal to 70 mg/dL
[b]Severe hypoglycemic events: requiring assistance regardless of blood glucose
[c]Treated set (patients who had received at least one dose of study drug)
[d]Insulin dose could not be adjusted during the initial 18 week treatment period

Genital Mycotic Infections: In the pool of five placebo-controlled clinical trials, the incidence of genital mycotic infections (e.g., vaginal mycotic infection, vaginal infection, genital infection fungal, vulvovaginal candidiasis, and vulvitis) was increased in patients treated with JARDIANCE compared to placebo, occurring in 0.9%, 4.1%, and 3.7% of patients randomized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. Discontinuation from study due to genital infection occurred in 0% of placebo-treated patients and 0.2% of patients treated with either JARDIANCE 10 or 25 mg. Genital mycotic infections occurred more frequently in female than male patients (see Table 1). Phimosis occurred more frequently in male patients treated with JARDIANCE 10 mg (less than 0.1%) and JARDIANCE 25 mg (0.1%) than placebo (0%). *Urinary Tract Infections:* In the pool of five placebo-controlled clinical trials, the incidence of urinary tract infections (e.g., urinary tract infection, asymptomatic bacteriuria, and cystitis) was increased in patients treated with JARDIANCE compared to placebo (see Table 1). Patients with a history of chronic or recurrent urinary tract infections were more likely to experience a urinary tract infection. The rate of treatment discontinuation due to urinary tract infections was 0.1%, 0.2%, and 0.1% for placebo,JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. Urinary tract infections occurred more frequently in female patients. The incidence of urinary tract infections in female patients randomized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg was 16.6%, 18.4%, and 17.0%, respectively. The incidence of urinary tract infections in male patients randomized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg was 3.2%, 3.6%, and 4.1%, respectively *[see Use in Specific Populations]*. Clinical Trials in Patients with Heart Failure: The EMPEROR-Reduced study included 3730 patients with heart failure and left ventricular ejection fraction (LVEF) ≤40% followed for a median of 16 months, and EMPEROR-Preserved included 5988 patients with heart failure and LVEF >40% followed for a median of 26 months. In both studies, patients were randomized to JARDIANCE 10 mg or placebo. The safety profile in patients with heart failure was generally consistent with that observed in patients with type 2 diabetes mellitus. *Laboratory Tests:* Increases in Serum Creatinine and Decreases in eGFR: Initiation of JARDIANCE causes an increase in serum creatinine and decrease in eGFR within weeks of starting therapy and then these changes stabilize. In a study of patients with moderate renal impairment, larger mean changes were observed. In a long-term cardiovascular outcomes trial, the increase in serum creatinine and decrease in eGFR generally did not exceed 0.1 mg/dL and -9.0 mL/min/1.73 m^2, respectively, at Week 4, and reversed after treatment discontinuation, suggesting acute hemodynamic changes may play a role in the renal function changes observed with JARDIANCE. Increase in Low-Density Lipoprotein Cholesterol (LDL-C): Dose-related increases in low-density lipoprotein cholesterol (LDL-C) were observed in patients treated with JARDIANCE. LDL-C increased by 2.3%, 4.6%, and 6.5% in patients treated with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. The range of mean baseline LDL-C levels was 90.3 to 90.6 mg/dL across treatment groups. Increase in Hematocrit: In a pool of four placebo-controlled studies, median hematocrit decreased by 1.3% in placebo and increased by 2.8% in JARDIANCE 10 mg and 2.8% in JARDIANCE 25 mg treated patients. At the end of treatment, 0.6%, 2.7%, and 3.5% of patients with hematocrits initially within the reference range had values above the upper limit of the reference range with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. **Postmarketing Experience:** Additional adverse reactions have been identified during postapproval use of JARDIANCE. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. *Gastrointestinal Disorders:* Constipation; *Infections:* Necrotizing fasciitis of the perineum (Fournier's gangrene), urosepsis and pyelonephritis; *Metabolism and Nutrition Disorders:* Ketoacidosis; *Renal and Urinary Disorders:* Acute kidney injury; *Skin and Subcutaneous Tissue Disorders:* Angioedema, skin reactions (e.g., rash, urticaria).

DRUG INTERACTIONS:

Table 3: Clinically Relevant Interactions with JARDIANCE

Diuretics	
Clinical Impact	Coadministration of empagliflozin with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion.
Intervention	Before initiating JARDIANCE, assess volume status and renal function. In patients with volume depletion, correct this condition before initiating JARDIANCE. Monitor for signs and symptoms of volume depletion, and renal function after initiating therapy.
Insulin or Insulin Secretagogues	
Clinical Impact	The risk of hypoglycemia is increased when JARDIANCE is used in combination with insulin secretagogues (e.g., sulfonylurea) or insulin.
Intervention	Coadministration of JARDIANCE with an insulin secretagogue (e.g., sulfonylurea) or insulin may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.
Positive Urine Glucose Test	
Clinical Impact	SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests.
Intervention	Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.
Interference with 1,5-anhydroglucitol (1,5-AG) Assay	
Clinical Impact	Measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors.
Intervention	Monitoring glycemic control with 1,5-AG assay is not recommended. Use alternative methods to monitor glycemic control.

USE IN SPECIFIC POPULATIONS: Pregnancy: *Risk Summary:* Based on animal data showing adverse renal effects, JARDIANCE is not recommended during the second and third trimesters of pregnancy. The limited available data with JARDIANCE in pregnant women are not sufficient to determine a drug-associated risk for major birth defects and miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy *[see Clinical Considerations]*. In animal studies, adverse renal changes were observed in rats when empagliflozin was administered during a period of renal development corresponding to the late second and third trimesters of human pregnancy. Doses approximately 13-times the maximum clinical dose caused renal pelvic and tubule dilatations that were reversible *[see Data]*. The estimated background risk of major birth defects is 6% to 10% in women with pre-gestational diabetes with a HbA1c >7 and has been reported to be as high as 20% to 25% in women with HbA1c >10. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Clinical Considerations: *Disease-associated maternal and/or embryo/fetal risk:* Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity. *Data:* Animal Data: Empagliflozin dosed directly to juvenile rats from postnatal day (PND) 21 until PND 90 at doses of 1, 10, 30 and 100 mg/kg/day caused increased kidney weights and renal tubular and pelvic dilatation at 100 mg/kg/day, which approximates 13-times the maximum clinical dose of 25 mg, based on AUC. These findings were not observed after a 13-week, drug-free recovery period. These outcomes occurred with drug exposure during periods of renal development in rats that correspond to the late second and third trimester of human renal development. In embryo-fetal development studies in rats and rabbits, empagliflozin was administered for intervals coinciding with the first trimester period of organogenesis in humans. Doses up to 300 mg/kg/day, which approximates 48-times (rats) and 128-times (rabbits) the maximum clinical dose of 25 mg (based on AUC), did not result in adverse developmental effects. In rats, at higher doses of empagliflozin

variables during the first 3 ICU days were extracted from electronic medical records. Four machine learning algorithms—logistic regression, random forest, support vector machine, and extreme gradient boost—were used to train the models for prediction of in-hospital death and major adverse kidney events (MAKEs). The latter outcome was a composite of death, renal replacement therapy, and 50% or greater reduction in estimated glomerular filtration rate from baseline to 120 days after discharge.

The developed clinical models included 15 features for prediction of mortality and 14 for prediction of MAKEs. Predictive performance was evaluated using tenfold cross-validation in the derivation cohort, followed by external validation of 2333 patients from a different center.

The 15-variable clinical model outperformed the Sequential Organ Failure Assessment score for prediction of mortality in both the derivation cohort (area under the curve [AUC], 0.79 vs. 0.71) and the validation cohort (AUC, 0.71 vs. 0.74). In the validation cohort, among patients classified as being at >50% predicted risk of mortality, 41% actually died.

The 14-variable model also improved prediction of MAKEs compared with the maximum AKI KDIGO score (AUC, 0.78 vs. 0.66 in the derivation cohort and 0.66 vs. 0.73 in the validation cohort). Among patients at 50% or higher risk, 24.5% developed a MAKE.

AKI occurs in up to 50% of patients admitted to the ICU. Although clinical models are useful in predicting AKI risk, there are few tools for prediction of AKI recovery or outcomes.

The newly developed models perform well in predicting in-hospital mortality and MAKEs in a heterogeneous population of ICU patients with AKI. "[I]f further validated, [the models] could enable risk stratification for timely interventions that promote kidney recovery," the researchers conclude. They have developed an online tool for predicting outcomes in critically ill adults with incident AKI within the first 3 days of an ICU stay, available at http://phenomics.uky.edu/taki/ [Neyra JA, et al. Prediction of mortality and major adverse kidney events in critically ill patients with acute kidney injury. *Am J Kidney Dis*, published online ahead of print July 13, 2022. doi: 10.1053/j.ajkd.2022.06.004; https://www.ajkd.org/article/S0272-6386(22)00774-0/fulltext]. ■

Acetazolamide Improves Outcomes in Decompensated Heart Failure

In patients with acute decompensated heart failure with volume overload, adding acetazolamide to loop diuretic therapy increases the odds of successful decongestion, concludes a clinical trial report in *The New England Journal of Medicine*.

The multicenter Acetazolamide in Decompensated Heart Failure with Volume Overload (ADVOR) trial enrolled 519 hospitalized patients with acute decompensated heart failure (63% men; mean age, 78 years). Eligible patients had at least one clinical sign of volume overload (e.g., edema, pleural effusion, or ascites); an N-terminal pro-B-type natriuretic peptide level >1000 pg/mL or B-type natriuretic peptide level >250 pg/mL; and at least 1 month of oral maintenance therapy with furosemide 40 mg or equivalent.

Patients were randomly assigned to acetazolamide, 500 mg intravenously (IV) once daily or placebo added to IV loop diuretics at a dose equivalent to twice the oral maintenance dose. Groups were stratified based on left ventricular ejection fraction with a cutoff of 40%. The main outcome of interest was successful decongestion, defined as no evidence of volume overload within 3 days after randomization with no indications for escalated decongestive therapy.

Acetazolamide was associated with a significant increase in successful decongestion compared with placebo (42.2% vs. 30.5%; risk ratio, 1.46). Patients assigned to acetazolamide had a nonsignificant reduction in a composite secondary outcome of all-cause mortality or heart failure rehospitalization (29.7% and 27.8%, respectively).

The acetazolamide group showed evidence of increased diuretic efficiency with higher cumulative urine output and natriuresis. Rates of worsening kidney function, hypokalemia, hypotension, or adverse events were similar between groups.

Even with high-dose loop diuretics, many patients with acute decompensated heart failure continued signs of volume overload after discharge, associated with poor clinical outcomes. Added to loop diuretics, the carbonic anhydrase inhibitor acetazolamide reduces proximal tubular sodium reabsorption and thus, might improve diuretic efficiency.

The ADVOR results show an increase in successful decongestion with acetazolamide added to standardized loop diuretic therapy for acute decompensated heart failure with volume overload. "These findings highlight the importance of targeting congestion both early and aggressively and support the use of natriuresis as an indicator of diuretic response," the researchers write [Mullens W, et al. Acetazolamide in acute decompensated heart failure with volume overload. *N Engl J Med*, published online ahead of print August 27, 2022. doi: 10.1056/NEJMoa2203094; https://www.nejm.org/doi/10.1056/NEJMoa2203094]. ■

WHEN TREATING HYPERKALEMIA

GO WITH LOKELMA

CHOOSE THE PATH TO RAPID* AND SUSTAINED† K^+ CONTROL[1,2]

In a retrospective analysis of a 12-month study,

89% OF PATIENTS CONTINUED RAAS INHIBITOR USE‡[3]

LEARN MORE ABOUT THE #1 PRESCRIBED K^+ BINDER BY NEPHROLOGISTS[4] AT LOKELMA-HCP.COM

LOKELMA®
(sodium zirconium cyclosilicate)
5 g | 10 g for oral suspension

INDICATION AND LIMITATION OF USE

LOKELMA is indicated for the treatment of hyperkalemia in adults.

LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

AstraZeneca

*In Study 1, LOKELMA 10 g tid demonstrated a greater reduction in serum K^+ levels vs placebo at 48 hours (*P*<0.001) and started to work as early as 1 hour in patients with hyperkalemia not on dialysis.[1,2]

†In Study 2, patients with hyperkalemia who achieved normokalemia with LOKELMA in the 48-hour initial phase entered into the 28-day maintenance phase, where those who continued LOKELMA maintained lower mean serum K^+ levels vs those who switched to placebo, with a greater proportion of patients having mean serum K^+ in the normal range with LOKELMA vs placebo. Patients in Study 2 who continued into the open-label, 11-month extension phase sustained normokalemia with continued LOKELMA dosing.[1]

‡In a retrospective analysis of data from Study 3, 483 patients were receiving RAAS inhibitor at baseline. Of those patients, 74% maintained dose, 13% increased dose, 14% decreased dose, and 11% discontinued RAAS inhibitor use during the 12-month open-label trial. Patients were counted more than once if they required more than 1 RAAS inhibitor adjustment, so the total percentage across all 4 categories may exceed 100%.[3]

IMPORTANT SAFETY INFORMATION FOR LOKELMA

WARNINGS AND PRECAUTIONS:

- **Gastrointestinal Adverse Events in Patients with Motility Disorders:** Avoid LOKELMA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders. LOKELMA has not been studied in patients with these conditions and it may be ineffective and may worsen gastrointestinal conditions
- **Edema:** Each 5-g dose of LOKELMA contains approximately 400 mg of sodium, but the extent of absorption by the patient is unknown. In clinical trials of LOKELMA in patients who were not on dialysis, edema was observed and was generally mild to moderate in severity and was more commonly seen in patients treated with 15 g once daily. Monitor for signs of edema, particularly in patients who should restrict their sodium intake or are prone to fluid overload (eg, heart failure or renal disease). Advise patients to adjust dietary sodium, if appropriate. Increase the dose of diuretics as needed

  In a clinical trial of LOKELMA in patients on chronic hemodialysis in which most patients were treated with doses of 5 g to 10 g once daily on non-dialysis days, there was no difference in the mean change from baseline in interdialytic weight gain (a measure of fluid retention) between the LOKELMA and placebo groups
- **Hypokalemia in Patients on Hemodialysis:** Patients on hemodialysis may be prone to acute illness that can increase the risk of hypokalemia on LOKELMA (eg, illnesses associated with decreased oral intake, diarrhea). Consider adjusting LOKELMA dose based on potassium levels in these settings
- **Diagnostic Tests:** LOKELMA has radio-opaque properties and, therefore, may give the appearance typical of an imaging agent during abdominal X-ray procedures

ADVERSE REACTIONS: The most common adverse reaction in non-dialysis patients with LOKELMA was mild to moderate edema. In placebo-controlled trials up to 28 days, edema was reported in 4.4%, 5.9%, 16.1% of non-dialysis patients treated with 5 g, 10 g, and 15 g of LOKELMA once daily, respectively vs 2.4% of non-dialysis patients receiving placebo.

DRUG INTERACTIONS: LOKELMA can transiently increase gastric pH. In general, oral medications with pH-dependent solubility should be administered at least 2 hours before or 2 hours after LOKELMA. Spacing is not needed if it has been determined the concomitant medication does not exhibit pH-dependent solubility.

Please read Brief Summary of Prescribing Information on adjacent page.

References: 1. LOKELMA® (sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2021. **2.** Packham DK, Rasmussen HS, Lavin PT, et al. Sodium zirconium cyclosilicate in hyperkalemia [article and supplementary material]. *N Engl J Med*. 2015;372(3):222-231. **3.** Spinowitz BS, Fishbane S, Pergola PE, et al; ZS-005 Study Investigators. Sodium zirconium cyclosilicate among individuals with hyperkalemia: a 12-month phase 3 study. *Clin J Am Soc Nephrol*. 2019;14(6):798-809. **4.** Data on file, US-53732, AZPLP.

LOKELMA® (sodium zirconium cyclosilicate) for oral suspension

Brief Summary of Prescribing Information.
For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

LOKELMA is indicated for the treatment of hyperkalemia in adults.

Limitation of Use

LOKELMA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action *[see Clinical Pharmacology (12.2) and Clinical Studies (14) in the full Prescribing Information]*.

DOSAGE AND ADMINISTRATION

Recommended Dosage

For initial treatment of hyperkalemia, the recommended dose of LOKELMA is 10 g administered three times a day for up to 48 hours. Administer LOKELMA orally as a suspension in water *[see Dosage and Administration (2.3) in the full Prescribing Information]*.

For continued treatment, the recommended dose is 10 g once daily. Monitor serum potassium and adjust the dose of LOKELMA based on the serum potassium level and desired target range. During maintenance treatment, up-titrate based on the serum potassium level at intervals of 1-week or longer and in increments of 5 g. Decrease the dose of LOKELMA or discontinue if the serum potassium is below the desired target range. The recommended maintenance dose range is from 5 g every other day to 15 g daily.

Dosage Adjustment for Patients on Chronic Hemodialysis

For patients on chronic hemodialysis, administer LOKELMA only on non-dialysis days.

The recommended starting dose is 5 g once daily on non-dialysis days. Consider a starting dose of 10 g once daily on non-dialysis days in patients with serum potassium greater than 6.5 mEq/L. Monitor serum potassium and adjust the dose of LOKELMA based on the pre-dialysis serum potassium value after the long inter-dialytic interval and desired target range.

During initiation and after a dose adjustment, assess serum potassium after one week. The recommended maintenance dose range is from 5 g to 15 g once daily, on non-dialysis days.

Discontinue or decrease the dose of LOKELMA if:

- serum potassium falls below the desired target range based on the pre-dialysis value after the long interdialytic interval, or;
- the patient develops clinically significant hypokalemia

Reconstitution and Administration

In general, other oral medications should be administered at least 2 hours before or 2 hours after LOKELMA *[see Drug Interactions (7) in the full Prescribing Information]*.

Instruct patients to empty the entire contents of the packet(s) into a drinking glass containing approximately 3 tablespoons of water or more if desired. Stir well and drink immediately. If powder remains in the drinking glass, add water, stir and drink immediately. Repeat until no powder remains to ensure the entire dose is taken.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Gastrointestinal Adverse Events in Patients with Motility Disorders

Avoid use of LOKELMA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders, because LOKELMA has not been studied in patients with these conditions and may be ineffective and may worsen gastrointestinal conditions.

Edema

Each 5 g dose of LOKELMA contains approximately 400 mg of sodium, but the extent of absorption by the patient is unknown. In clinical trials of LOKELMA in patients who were not on dialysis, edema was observed and was generally mild to moderate in severity and was more commonly seen in patients treated with 15 g once daily. Monitor for signs of edema, particularly in patients who should restrict their sodium intake or are prone to fluid overload (e.g., heart failure or renal disease). Advise patients to adjust dietary sodium, if appropriate. Increase the dose of diuretics as needed *[see Adverse Reactions (6) in the full Prescribing Information]*.

In a clinical trial of LOKELMA in patients on chronic hemodialysis in which most patients were treated with doses of 5 to 10 g once daily on non-dialysis days, there was no difference in the mean change from baseline in interdialytic weight gain (a measure of fluid retention) between the LOKELMA and placebo groups.

Hypokalemia in Patients on Hemodialysis

Patients on hemodialysis may be prone to acute illness that can increase the risk of hypokalemia on LOKELMA (e.g., illnesses associated with decreased oral intake, diarrhea). Consider adjusting Lokelma dose based on potassium levels in these settings.

Diagnostic Tests

LOKELMA has radio-opaque properties and, therefore, may give the appearance typical of an imaging agent during abdominal X-ray procedures.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the label:

- Edema *[see Warnings and Precautions (5.2) in the full Prescribing Information]*.

Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The total exposure to LOKELMA in the safety and efficacy clinical trials of patients not on dialysis with hyperkalemia was 1,760 patients with 652 patients exposed to LOKELMA for at least 6 months and 507 patients exposed for at least one year.

The population (n=1,009) in the placebo-controlled trials included patients aged 22 to 96 years, females (n=454), Caucasians (n=859) and Blacks (n=130). Patients had hyperkalemia in association with comorbid diseases such as chronic kidney disease, heart failure, and diabetes mellitus.

In placebo-controlled trials in which patients who were not on dialysis were treated with once daily doses of LOKELMA for up to 28 days, edema was reported in 4.4% of patients receiving 5 g, 5.9% of patients receiving 10 g and 16.1% of patients receiving 15 g LOKELMA compared to 2.4% of patients receiving placebo. In longer-term uncontrolled trials in which most patients were maintained on doses <15 g once daily, adverse reactions of edema (edema, generalized edema and peripheral edema) were reported in 8% to 11% of patients.

Laboratory Abnormalities

In clinical trials in patients who were not on dialysis, 4.1% of LOKELMA-treated patients developed hypokalemia with a serum potassium value less than 3.5 mEq/L, which resolved with dosage reduction or discontinuation of LOKELMA. In a clinical trial of LOKELMA in patients on chronic hemodialysis, 5% of patients developed pre-dialysis hypokalemia (serum potassium <3.5 mEq/L) in both the LOKELMA and placebo groups; 3% and 1% of patients developed a serum potassium < 3.0 mEq/L in the LOKELMA and placebo groups, respectively.

DRUG INTERACTIONS

LOKELMA can transiently increase gastric pH. As a result, LOKELMA can change the absorption of co-administered drugs that exhibit pH-dependent solubility, potentially leading to altered efficacy or safety of these drugs when taken close to the time LOKELMA is administered. In general, other oral medications should be administered at least 2 hours before or 2 hours after LOKELMA *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3) in the full Prescribing Information]*. LOKELMA is not expected to impact systemic exposure of drugs that do not exhibit pH-dependent solubility and so spacing is not needed if it has been determined that the concomitant medication does not exhibit pH-dependent solubility.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

LOKELMA is not absorbed systemically following oral administration and maternal use is not expected to result in fetal exposure to the drug.

Lactation

Risk Summary

LOKELMA is not absorbed systemically following oral administration, and breastfeeding is not expected to result in exposure of the child to LOKELMA.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total number of subjects in clinical studies of LOKELMA, 58% were age 65 and over, while 25% were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients.

PATIENT COUNSELING INFORMATION

Dosing

Instruct the patient how to reconstitute LOKELMA for administration. Inform the patient that it is necessary to drink the full dose *[see Dosage and Administration (2.3) in the full Prescribing Information]*.

Instruct dialysis patients who experience acute illness (e.g., decreased oral intake of food or fluids, diarrhea) to contact the health care provider. The dose of LOKELMA may need to be adjusted *[see Warnings and Precautions (5.3) in the full Prescribing Information]*.

Diagnostic Testing

Advise patients to notify their physician prior to an abdominal X-ray *[see Warnings and Precautions (5.4) in the full Prescribing Information]*.

Drug Interactions

Advise patients who are taking other oral medications to separate dosing of LOKELMA by at least 2 hours (before or after) *[see Drug Interactions (7) in the full Prescribing Information]*.

Diet

Advise patients to adjust dietary sodium, if appropriate *[see Warnings and Precautions (5.2) in the full Prescribing Information]*.

U.S. Patent No: 6332985, 8808750, 8877255, 8802152, 9592253

Manufactured by: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

10/21 US-59088 11/21

The Risk of Hematuria and Proteinuria with Rosuvastatin Use in Severe CKD

By Zainab Obaidi and Marco Bonilla

Statin therapy has been on the rise in patients with chronic kidney disease (CKD) following the National Kidney Foundation and American Heart Association guidelines recognizing CKD as a cardiovascular risk equivalent for atherosclerotic cardiovascular disease prevention (1, 2). Several clinical and basic sciences studies have noted the benefits of statin use, such as renovascular protection and delaying fibrosis (3–7). However, adverse effects, such as hematuria and proteinuria, have been reported with high-dose rosuvastatin use since its approval by the U.S. Food and Drug Administration (FDA) in 2003 (8, 9). The reported incidence of proteinuria was <1% and <1.5% in rosuvastatin, 5–10 mg dose versus 40 mg dose, respectively (9). A recent large observational cohort study by Shin et al. (10), published in *JASN*, examined the association of hematuria and proteinuria risk with rosuvastatin versus atorvastatin use.

The investigators compared approximately 1 million new statin users (n = 152,101 rosuvastatin and n = 795,799 atorvastatin) during a median follow-up of 3 years, using a database of 40 health care electronic medical records in the United States from 2011 to 2019. Eligibility criteria included patients with no prior hematuria or proteinuria, patients' recent labs (creatinine, glomerular filtration rate [GFR], urine albumin-to-creatinine ratio [UACR], or urine protein-to-creatinine ratio), and patients new to statin therapy (within 1 year). Patients were excluded if they had missing or no labs and/or kidney failure with replacement therapy or evidence or rhabdomyolysis.

Both groups had similar baseline characteristics with a mean age of 60 years, 82% White, 28% with diabetes, 66% with hypertension, and 10% with coronary artery disease. Hematuria (defined as dipstick hematuria ≥1+ or the presence of three or more red blood cells in urine microscopy noted at more than two separate time points) occurred in 5178 individuals (3.4%) in the rosuvastatin group versus 22,604 individuals (2.8%) in the atorvastatin group over a 3-year follow-up. The incidence rate of hematuria among patients with estimated GFR (eGFR) <30 mL/min/1.73 m^2 was twofold higher than those with eGFR >60 mL/min/1.73 m^2 (8.4 events for rosuvastatin vs 7.9 events for atorvastatin per 1000 person-years).

For the risk of proteinuria (defined as dipstick proteinuria ≥2+ or UACR ≥300 mg/g noted at more than two separate timepoints), the incidence rates were 1.2% (n = 1776) for rosuvastatin and 0.9% (n = 7495) for atorvastatin, with a ninefold greater risk for patients with eGFR <30 mL/min/1.73 m^2. Eighty percent of patients with an eGFR <30 mL/min/1.73 m^2 were started on a higher rosuvastatin dose than what is recommended as the initial dose by the FDA (5 mg). There was a greater risk of proteinuria and hematuria noted with higher rosuvastatin dosing and kidney failure with replacement therapy risk (inverse probability of treatment weighting [IPTW] hazard ratio, 1.15; 95% CI, 1.02–1.30) when compared with atorvastatin.

This study had several strengths. It used the IPTW within each of the 40 study cohorts to minimize confounders between the two treatment groups. This is one of the first studies that examined the risk of hematuria and proteinuria with high-intensity statins in a large CKD population. The authors noted some limitations to the study relating to the study population, as most individuals were insured, and <1% were with eGFR <30 mL/min/1.73 m^2, which limits its generalizability. In addition, other causes of proteinuria should be carefully examined, as approximately 60% of the study population had hypertension and diabetes, 30% were on angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and 1% was on sodium glucose co-transporter 2 inhibitors. Kidney biopsy was not performed to determine the cause of proteinuria or whether proteinuria resolved on discontinuation of the statins.

The association of rosuvastatin with proteinuria can also be related to its renal clearance (10%–25%) when compared with other statins that are hepatically metabolized (8, 11). In vitro studies' proposed mechanisms for proteinuria with statin use included a dose-dependent impaired albumin tubular absorption via receptor-mediated endocytosis in proximal tubules due to β-hydroxy β-methylglutaryl-coenzyme A reductase inhibition (12, 13). Another study noted oxidative stress leading to mitochondrial dysfunction due to reduced ubiquinone synthesis (14). van Zyl-Smit and colleagues (15) reported that a case of proteinuria and hematuria that resolved upon rosuvastatin discontinuation and kidney biopsy findings was notable for tubular casts and chronic tubulointerstitial kidney disease.

In conclusion, pharmacovigilance of rosuvastatin used in patients with severe CKD is of importance. The initial rosuvastatin dose should be reduced to 5 mg daily to a maximum dose of 10 mg daily in patients with severe CKD (eGFR <30 mL/min per 1.73 m^2). Adequate follow-up and patient education are required to monitor for adverse effects, such as proteinuria, hematuria, or acute kidney injury, during drug initiation. Nonetheless, further studies are needed to elucidate the effect of statins in severe kidney diseases. ■

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The authors report no conflicts of interest.

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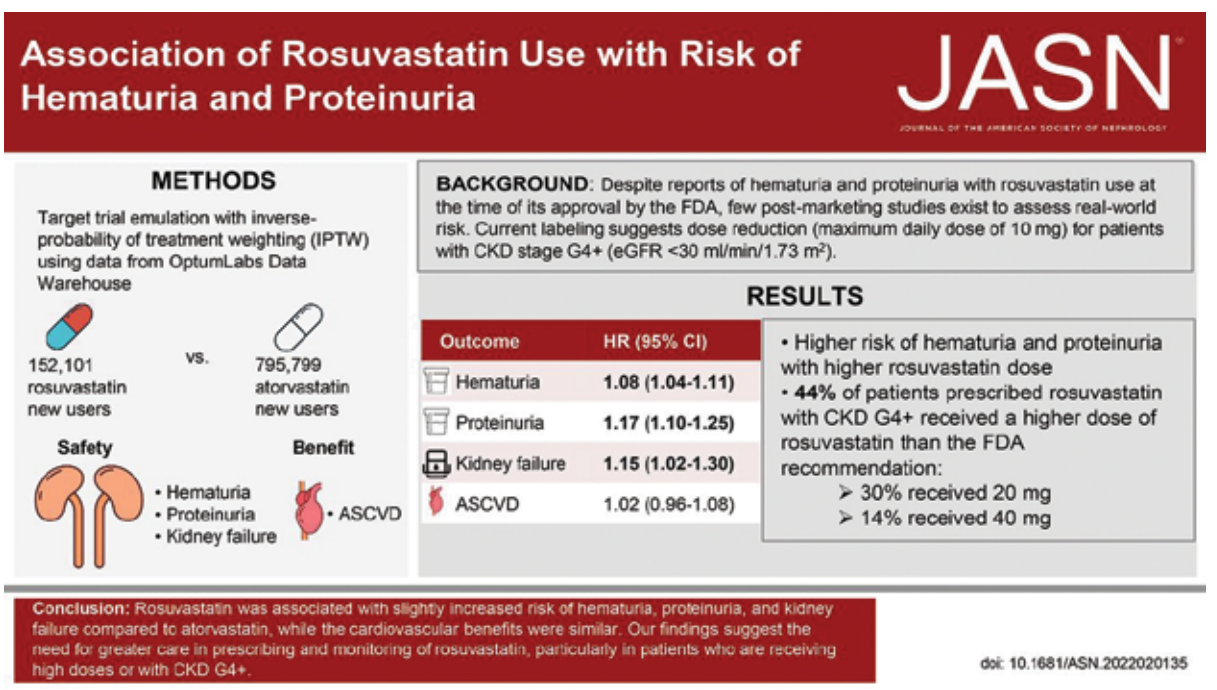

ASCVD, atherosclerotic cardiovascular disease; HR, hazard ratio; CI, confidence interval. Reprinted from Shin et al. (10).

NEW FDA-APPROVED DATA

KRYSTEXXA **can change the course** of uncontrolled gout[1]

KRYSTEXXA with methotrexate:

>80%
relative improvement in patient response;
71% (71/100) vs 39% (20/52) complete response* compared to KRYSTEXXA alone[1]

87%
relative reduction in infusion reactions;
4% (4/96) vs 31% (15/49) compared to KRYSTEXXA alone[1]

A 52-week, randomized, double-blind trial conducted in adult patients with chronic gout refractory to conventional therapy to evaluate administration of KRYSTEXXA 8 mg Q2W co-administered with 15 mg oral methotrexate QW and 1 mg oral folic acid QD vs KRYSTEXXA alone.[1,2]

QD, every day; QW, every week; Q2W, every 2 weeks.

*Complete sUA response: The primary efficacy endpoint was the proportion of responders, defined by patients achieving and maintaining sUA <6 mg/dL for at least 80% of the time during Month 6.[1]

INDICATION

KRYSTEXXA® (pegloticase) is indicated for the treatment of chronic gout in adult patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Limitations of Use: KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

IMPORTANT SAFETY INFORMATION

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS, G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

- **Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.**
- **Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. Delayed hypersensitivity reactions have also been reported.**
- **KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.**
- **Premedicate with antihistamines and corticosteroids and closely monitor for anaphylaxis for an appropriate period after administration of KRYSTEXXA.**
- **Monitor serum uric acid levels prior to each infusion and discontinue treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.**
- **Screen patients at risk for glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. KRYSTEXXA is contraindicated in patients with G6PD deficiency.**

CONTRAINDICATIONS:

- In patients with G6PD deficiency.
- In patients with history of serious hypersensitivity reactions, including anaphylaxis, to KRYSTEXXA or any of its components.

Dissolve years of systemic urate deposition[3]
ChangeTheCourse.com

WARNINGS AND PRECAUTIONS

Gout Flares: An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including KRYSTEXXA. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

Congestive Heart Failure: KRYSTEXXA has not been formally studied in patients with congestive heart failure, but some patients in the pre-marketing placebo-controlled clinical trials experienced exacerbation. Exercise caution in patients who have congestive heart failure and monitor patients closely following infusion.

ADVERSE REACTIONS

The most commonly reported adverse reactions (≥5%) are:

KRYSTEXXA co-administration with methotrexate trial:
KRYSTEXXA with methotrexate: gout flares, arthralgia, COVID-19, nausea, and fatigue; KRYSTEXXA alone: gout flares, arthralgia, COVID-19, nausea, fatigue, infusion reaction, pain in extremity, hypertension, and vomiting.

KRYSTEXXA pre-marketing placebo-controlled trials:
gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis, and vomiting.

Please see Brief Summary of Prescribing Information for KRYSTEXXA on following page.

References: 1. KRYSTEXXA (pegloticase) [prescribing information] Horizon. **2.** Botson J, et al. *J Clin Rheumatol*. 2022;28:e129-e134. **3.** Data on File. Horizon, March 2022.

HORIZON.

KRYSTEXXA®
pegloticase

KRYSTEXXA® (pegloticase) injection, for intravenous use

Brief Summary - Please see the KRYSTEXXA package insert for Full Prescribing Information.

WARNING: ANAPHYLAXIS and INFUSION REACTIONS, G6PD DEFICIENCY ASSOCIATED HEMOLYSIS and METHEMOGLOBINEMIA

See full prescribing information for complete boxed warning.

- **Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.**
- **Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed hypersensitivity reactions have also been reported.**
- **KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.**
- **Pre-medicate with antihistamines and corticosteroids and closely monitor for anaphylaxis for an appropriate period of time after administration of KRYSTEXXA.**
- **Monitor serum uric acid levels prior to each infusion and discontinue treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.**
- **Screen patients at risk for G6PD deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. KRYSTEXXA is contraindicated in patients with G6PD deficiency.**

INDICATIONS AND USAGE

KRYSTEXXA® (pegloticase) is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Limitations of Use:
KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

CONTRAINDICATIONS

KRYSTEXXA is contraindicated in:

- Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency *[see Warnings and Precautions]*
- Patients with history of serious hypersensitivity reactions, including anaphylaxis, to KRYSTEXXA or any of its components

WARNINGS AND PRECAUTIONS

Anaphylaxis

In a 52-week controlled trial, which evaluated KRYSTEXXA co-administered with methotrexate compared to KRYSTEXXA alone, patients were pre-treated with standardized infusion reaction prophylaxis and were discontinued from treatment with KRYSTEXXA if serum uric acid levels increased to above 6 mg/dL at 2 consecutive visits after the initiation of KRYSTEXXA therapy to reduce the risk of anaphylaxis. One patient randomized to the group treated with KRYSTEXXA co-administered with methotrexate (1%) experienced anaphylaxis during the first infusion and no patients experienced anaphylaxis in the group treated with KRYSTEXXA alone *[see Adverse Reactions]*.

During pre-marketing clinical trials with KRYSTEXXA alone, KRYSTEXXA was not discontinued following 2 consecutive serum uric acid levels above 6 mg/dL. Anaphylaxis was reported with a frequency of 6.5% (8/123) of patients treated with KRYSTEXXA every 2 weeks and 4.8% (6/126) for the every 4-week dosing regimen. There were no cases of anaphylaxis in patients receiving placebo. Anaphylaxis generally occurred within 2 hours after treatment.

Diagnostic criteria of anaphylaxis were skin or mucosal tissue involvement, and, either airway compromise, and/or reduced blood pressure with or without associated symptoms, and a temporal relationship to KRYSTEXXA or placebo injection with no other identifiable cause. Manifestations included wheezing, peri-oral or lingual edema, or hemodynamic instability, with or without rash or urticaria, nausea or vomiting. Cases occurred in patients being pre-treated with one or more doses of an oral antihistamine, an intravenous corticosteroid and/or acetaminophen. This pre-treatment may have blunted or obscured symptoms or signs of anaphylaxis and therefore the reported frequency may be an underestimate.

KRYSTEXXA should be administered in a healthcare setting by healthcare providers prepared to manage anaphylaxis. Patients should be pre-treated with antihistamines and corticosteroids. Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed type hypersensitivity reactions have also been reported. Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA. Patients should be informed of the symptoms and signs of anaphylaxis and instructed to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.

The risk of anaphylaxis is higher in patients whose uric acid level increases to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed. Monitor serum uric acid levels prior to infusions and discontinue treatment if levels increase to above 6 mg/dL. Because of the possibility that concomitant use of oral urate-lowering therapy and KRYSTEXXA may potentially blunt the rise of serum uric acid levels, it is recommended that before starting KRYSTEXXA patients discontinue oral urate-lowering medications and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

Infusion Reactions

In a 52-week, controlled trial which evaluated KRYSTEXXA co-administered with methotrexate compared to KRYSTEXXA alone *[see Adverse Reactions]*, patients were pre-treated with standardized infusion reaction prophylaxis and were discontinued from treatment with KRYSTEXXA if serum uric acid levels increased to above 6 mg/dL at 2 consecutive visits after the initiation of KRYSTEXXA therapy to reduce the risk of infusion reactions. Infusion reactions were reported in 4% of patients in the KRYSTEXXA co-administered with methotrexate group compared to 31% of patients treated with KRYSTEXXA alone experienced infusion reactions *[see Adverse Reactions]*. In both treatment groups, the majority of infusion reactions occurred at the first or second KRYSTEXXA infusion and during the time of infusion. Manifestations of these infusion reactions were similar to that observed in the pre-marketing trials.

During pre-marketing 24-week controlled clinical trials with KRYSTEXXA alone, KRYSTEXXA was not discontinued following 2 consecutive serum uric acid levels above 6 mg/dL. Infusion reactions were reported in 26% of patients treated with KRYSTEXXA 8 mg every 2 weeks, and 41% of patients treated with KRYSTEXXA 8 mg every 4 weeks, compared to 5% of patients treated with placebo. These infusion reactions occurred in patients being pre-treated with an oral antihistamine, intravenous corticosteroid and/or acetaminophen. This pre-treatment may have blunted or obscured symptoms or signs of infusion reactions and therefore the reported frequency may be an underestimate.

Manifestations of these reactions included urticaria (frequency of 10.6%), dyspnea (frequency of 7.1%), chest discomfort (frequency of 9.5%), chest pain (frequency of 9.5%), erythema (frequency of 9.5%), and pruritus (frequency of 9.5%). These manifestations overlap with the symptoms of anaphylaxis, but in a given patient did not occur together to satisfy the clinical criteria for diagnosing anaphylaxis. Infusion reactions are thought to result from release of various mediators, such as cytokines. Infusion reactions occurred at any time during a course of treatment with approximately 3% occurring with the first infusion, and approximately 91% occurred during the time of infusion.

KRYSTEXXA should be administered in a healthcare setting by healthcare providers prepared to manage infusion reactions. Patients should be pre-treated with antihistamines and corticosteroids. KRYSTEXXA should be infused slowly over no less than 120 minutes. In the event of an infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate.

The risk of infusion reaction is higher in patients whose uric acid level increases to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed. Monitor serum uric acid levels prior to infusions and discontinue treatment if levels increase to above 6 mg/dL. Because of the possibility that concomitant use of oral urate-lowering therapy and KRYSTEXXA may potentially blunt the rise of serum uric acid levels, it is recommended that before starting KRYSTEXXA patients discontinue oral urate-lowering medications and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

G6PD Deficiency Associated Hemolysis and Methemoglobinemia

Life threatening hemolytic reactions and methemoglobinemia have been reported with KRYSTEXXA in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Because of the risk of hemolysis and methemoglobinemia, do not administer KRYSTEXXA to patients with G6PD deficiency *[see Contraindications]*. Screen patients at risk for G6PD deficiency prior to starting KRYSTEXXA. For example, patients of African, Mediterranean (including Southern European and Middle Eastern), and Southern Asian ancestry are at increased risk for G6PD deficiency.

Gout Flares

In a 52-week, randomized, double-blind trial which evaluated KRYSTEXXA co-administered with methotrexate compared to KRYSTEXXA alone, patients were administered gout flare prophylaxis similar to that in the pre-marketing, placebo-controlled trials.

In this trial, the percentages of patients with any flare for the first 3 months were 66% and 69% for the group treated with KRYSTEXXA co-administered with methotrexate and the group treated with KRYSTEXXA alone, respectively. In the group treated with KRYSTEXXA co-administered with methotrexate, the percentages of patients with any flare for the subsequent 3 month increments of treatment were 27% during Month 6, 8% during Month 9 and 9% during Month 12. In the group treated with KRYSTEXXA alone, the percentages of patients with any flare were 14% during Month 6, 9% during Month 9 and 21% during Month 12.

During pre-marketing, 24-week controlled clinical trials with KRYSTEXXA alone, the frequencies of gout flares were high in all treatment groups, but more so with KRYSTEXXA treatment during the first 3 months of treatment, and decreased in the subsequent 3 months of treatment. The percentages of patients with any flare for the first 3 months were 74%, 81%, and 51%, for KRYSTEXXA 8 mg every 2 weeks, KRYSTEXXA 8 mg every 4 weeks, and placebo, respectively. The percentages of patients with any flare for the subsequent 3 months were 41%, 57%, and 67%, for KRYSTEXXA 8 mg every 2 weeks, KRYSTEXXA 8 mg every 4 weeks, and placebo, respectively. Patients received gout flare prophylaxis with colchicine and/or nonsteroidal anti-inflammatory drugs (NSAIDs) starting at least one week before receiving KRYSTEXXA.

Gout flares may occur after initiation of KRYSTEXXA. An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, due to changing serum uric acid levels resulting in mobilization of urate from tissue deposits. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated. KRYSTEXXA does not need to be discontinued because of a gout flare. The gout flare should be managed concurrently as appropriate for the individual patient *[see Dosage and Administration]*.

Congestive Heart Failure

KRYSTEXXA has not been formally studied in patients with congestive heart failure, but some patients in the pre-marketing, 24-week controlled clinical trials experienced exacerbation of congestive heart failure. Two cases of congestive heart failure exacerbation occurred during the trials in patients receiving treatment with KRYSTEXXA 8 mg every 2 weeks. No cases were reported in placebo-treated patients. Four subjects had exacerbations of pre-existing congestive heart failure while receiving KRYSTEXXA 8 mg every 2 weeks during the open-label extension study.

Exercise caution when using KRYSTEXXA in patients who have congestive heart failure and monitor patients closely following infusion.

Re-treatment with KRYSTEXXA

No controlled trial data are available on the safety and efficacy of re-treatment with KRYSTEXXA after stopping treatment for longer than 4 weeks. Due to the immunogenicity of KRYSTEXXA, patients receiving re-treatment may be at increased risk of anaphylaxis and infusion reactions. Therefore, patients receiving re-treatment after a drug-free interval should be monitored carefully *[see Adverse Reactions]*.

ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the label:

- Anaphylaxis *[see Warnings and Precautions]*
- Infusion Reactions *[see Warnings and Precautions]*
- G6PD Deficiency Associated Hemolysis and Methemoglobinemia *[see Warnings and Precautions]*
- Gout Flares *[see Warnings and Precautions]*
- Congestive Heart Failure *[see Warnings and Precautions]*

Clinical Trials Experience

Because clinical studies are conducted under widely varying and controlled conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug, and may not predict the rates observed in a broader patient population in clinical practice.

Co-administration with Methotrexate

A 52-week, randomized, double-blind trial was conducted in adult patients with chronic gout refractory to conventional therapy to evaluate administration of KRYSTEXXA 8 mg every 2 weeks co-administered with weekly administration of oral methotrexate 15 mg, compared to KRYSTEXXA alone. In this trial, patients who were able to tolerate two weeks on methotrexate 15 mg were then randomized to receive four additional weeks on either methotrexate 15 mg or matching placebo prior to initiating KRYSTEXXA therapy. A total of 152 subjects were randomized, and of these, 145 subjects completed the 4-week methotrexate run-in period and received KRYSTEXXA (96 subjects received KRYSTEXXA co-administered with methotrexate and 49 received KRYSTEXXA plus placebo) during the treatment period. All patients received pre-treatment with an oral antihistamine, intravenous corticosteroid and acetaminophen. These patients were between the ages of 24 and 83 years (average 55 years); 135 patients were male and 17 and were female; 105 patients were White/Caucasian, 22 were Black/African American,

14 were Asian, 5 were Native Hawaiian/Other Pacific Islander and 5 identified as Other; 28 were Hispanic or Latino. Common co-morbid conditions among the enrolled patients included hypertension (63%), osteoarthritis (25%), hyperlipidemia (24%), gastroesophageal reflux disease (22%), obesity (20%), type 2 diabetes (18%) and depression (16%). Patients with an eGFR <40 mL/min/1.73 m² were excluded from this trial.

The most commonly reported adverse reaction during the methotrexate pre-treatment periods was gout flare. The most commonly reported adverse reactions that occurred in ≥ 5% in either treatment group during the KRYSTEXXA co-administered with methotrexate or KRYSTEXXA alone period are provided in Table 1.

Table 1. Adverse Reactions Occurring in 5% or More of Patients in Either the KRYSTEXXA Co-administered with Methotrexate or KRYSTEXXA Alone Treatment Period

Adverse Reaction	KRYSTEXXA with Methotrexate (N=96) n (%)	KRYSTEXXA Alone (N=49) n (%)
Gout flare	64 (67%)	35 (71%)
Arthralgia	13 (14%)	5 (10%)
COVID-19	9 (9%)	3 (6%)
Nausea	5 (5%)	6 (12%)
Fatigue	5 (5%)	2 (4%)
Infusion reaction	4 (4%)[a]	15 (31%)
Pain in extremity	1 (1%)	3 (6%)
Hypertension	1 (1%)	3 (6%)
Vomiting	0	4 (8%)

[a] Included one case of anaphylaxis

KRYSTEXXA ALONE

The data described below reflect exposure to KRYSTEXXA in patients with chronic gout refractory to conventional therapy in two replicate randomized, placebo-controlled, double-blind 24-week clinical trials: 85 patients were treated with KRYSTEXXA 8 mg every 2 weeks; 84 patients were treated with KRYSTEXXA 8 mg every 4 weeks; and 43 patients were treated with placebo. These patients were between the ages of 23 and 89 years (average 55 years); 173 patients were male and 39 were female; and 143 patients were White/Caucasian, 27 were Black/African American, 24 were Hispanic/Latino and 18 were all other ethnicities. Common co-morbid conditions among the enrolled patients included hypertension (72%), dyslipidemia (49%), chronic kidney disease (28%), diabetes (24%), coronary artery disease (18%), arrhythmia (16%), and cardiac failure/left ventricular dysfunction (12%).

During the pre-marketing placebo-controlled clinical trials, the most commonly reported adverse reactions that occurred in greater than or equal to 5% of patients treated with KRYSTEXXA 8 mg every 2 weeks are provided in Table 2.

Table 2. Adverse Reactions Occurring in 5% or More of Patients Treated with KRYSTEXXA Compared to Placebo

Adverse Reaction	KRYSTEXXA 8 mg every 2 weeks (N=85) n[a] (%)	Placebo (N=43) n (%)
Gout flare	65 (77%)	35 (81%)
Infusion reaction	22 (26%)	2 (5%)
Nausea	10 (12%)	1 (2%)
Contusion[b] or Ecchymosis[b]	9 (11%)	2 (5%)
Nasopharyngitis	6 (7%)	1 (2%)
Constipation	5 (6%)	2 (5%)
Chest Pain	5 (6%)	1 (2%)
Anaphylaxis	4 (5%)	0 (0%)
Vomiting	4 (5%)	1 (2%)

[a] If the same subject in a given group had more than one occurrence in the same preferred term event category, the subject was counted only once.

[b] Most did not occur on the day of infusion and could be related to other factors (e.g., concomitant medications relevant to contusion or ecchymosis, insulin dependent diabetes mellitus).

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The observed incidence of antibody positivity in an assay is highly dependent on several factors including assay sensitivity and specificity and assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, the comparison of the incidence of antibodies to pegloticase with the incidence of antibodies to other products may be misleading.

In a 52-week, randomized, double-blind trial which evaluated KRYSTEXXA co-administered with methotrexate compared to KRYSTEXXA alone, approximately 26% of patients had pre-existing antibodies to pegloticase. Patients with an increase in titer from baseline or who were negative at baseline and developed an anti-pegloticase response at one or more post dose time points was 30% and 51%, for the KRYSTEXXA co-administered with methotrexate and KRYSTEXXA alone treatment groups, respectively. Patients with higher antibody titers were more likely to have faster clearance and lower efficacy.

During pre-marketing 24-week controlled clinical trials with KRYSTEXXA alone, anti-pegloticase antibodies developed in 92% of patients treated with KRYSTEXXA every 2 weeks, and 28% for placebo. Anti-PEG antibodies were also detected in 42% of patients treated with KRYSTEXXA. High anti-pegloticase antibody titer was associated with a failure to maintain pegloticase-induced normalization of uric acid. The impact of anti-PEG antibodies on patients' responses to other PEG-containing therapeutics is unknown.

There was a higher incidence of infusion reactions in patients with high anti-pegloticase antibody titer: 53% (16 of 30) in the KRYSTEXXA every 2 weeks group compared to 6% in patients who had undetectable or low antibody titers.

Postmarketing Experience

The following adverse reactions have been identified during postapproval use of KRYSTEXXA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship.

General disorders and administration site conditions: asthenia, malaise, peripheral swelling

DRUG INTERACTIONS

Methotrexate

KRYSTEXXA 8 mg every 2 weeks has been studied in patients with chronic gout refractory to conventional therapy taking concomitant oral methotrexate 15 mg weekly. Co-administration of methotrexate with KRYSTEXXA may increase pegloticase concentration compared to KRYSTEXXA alone.

PEGylated products

Because anti-pegloticase antibodies appear to bind to the PEG portion of the drug, there may be potential for binding with other PEGylated products. The impact of anti-PEG antibodies on patients' responses to other PEG-containing therapeutics is unknown.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate and well-controlled studies of KRYSTEXXA in pregnant women. Based on animal reproduction studies, no structural abnormalities were observed when pegloticase was administered by subcutaneous injection to pregnant rats and rabbits during the period of organogenesis at doses up to 50 and 75 times, respectively, the maximum recommended human dose (MRHD). Decreases in mean fetal and pup body weights were observed at approximately 50 and 75 times the MRHD, respectively *[see Data]*.

All pregnancies have a background risk of birth defect, loss or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinical recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In 2 separate embryo-fetal developmental studies, pregnant rats and rabbits received pegloticase during the period of organogenesis at doses up to approximately 50 and 75 times the maximum recommended human dose (MRHD), respectively (on a mg/m² basis at maternal doses up to 40 and 30 mg/kg twice weekly, in rats and rabbits, respectively). No evidence of structural abnormalities was observed in rats or rabbits. However, decreases in mean fetal and pup body weights were observed at approximately 50 and 75 times the MRHD in rats and rabbits, respectively (on a mg/m² basis at maternal doses up to 40 and 30 mg/kg every other day, in rats and rabbits, respectively). No effects on mean fetal body weights were observed at approximately 10 and 25 times the MRHD in rats and rabbits, respectively (on a mg/m² basis at maternal doses up to 10 mg/kg twice weekly in both species).

Lactation

Risk Summary

It is not known whether this drug is excreted in human milk. Therefore, KRYSTEXXA should not be used when breastfeeding unless the clear benefit to the mother can overcome the unknown risk to the newborn/infant.

Pediatric Use

The safety and effectiveness of KRYSTEXXA in pediatric patients less than 18 years of age have not been established.

Geriatric Use

Of the total number of patients treated with KRYSTEXXA 8 mg every 2 weeks in the controlled studies, 34% (29 of 85) were 65 years of age and older and 12% (10 of 85) were 75 years of age and older. No overall differences in safety or effectiveness were observed between older and younger patients, but greater sensitivity of some older individuals cannot be ruled out. No dose adjustment is needed for patients 65 years of age and older.

Renal Impairment

No dose adjustment is required for patients with renal impairment. In a 52-week, randomized, double-blind trial which evaluated KRYSTEXXA co-administered with methotrexate compared to KRYSTEXXA alone, 85% of patients had chronic kidney disease based on estimated glomerular filtration rate (eGFR) of ≥ 40 to < 90 mL/min/1.73 m² at baseline. In the pre-marketing 24-week controlled clinical trials with KRYSTEXXA alone, a total of 32% (27 of 85) of patients treated with KRYSTEXXA 8 mg every 2 weeks had a creatinine clearance of ≤62.5 mL/min. No overall differences in efficacy were observed.

OVERDOSAGE

No reports of overdosage with KRYSTEXXA have been reported. The maximum dose that has been administered as a single intravenous dose is 12 mg as uricase protein. Patients suspected of receiving an overdose should be monitored, and general supportive measures should be initiated as no specific antidote has been identified.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Anaphylaxis and Infusion Reactions

- Anaphylaxis and infusion reactions can occur at any infusion while on therapy. Counsel patients on the importance of adhering to any prescribed medications to help prevent or lessen the severity of these reactions.
- Educate patients on the signs and symptoms of anaphylaxis, including wheezing, peri-oral or lingual edema, hemodynamic instability, and rash or urticaria, nausea or vomiting.
- Educate patients on the most common signs and symptoms of an infusion reaction, including urticaria (skin rash), erythema (redness of the skin), dyspnea (difficulty breathing), flushing, chest discomfort, chest pain, and rash.
- Advise patients to seek medical care immediately if they experience any symptoms of an allergic reaction during or at any time after the infusion of KRYSTEXXA *[see Warnings and Precautions, Adverse Reactions]*
- Advise patients to discontinue any oral urate-lowering agents before starting on KRYSTEXXA and not to take any oral urate-lowering agents while on KRYSTEXXA.

Glucose-6-phosphate dehydrogenase (G6PD) Deficiency

Inform patients not to take KRYSTEXXA if they have a condition known as G6PD deficiency. Explain to patients that G6PD deficiency is more frequently found in individuals of African, Mediterranean, or Southern Asian ancestry and that they may be tested to determine if they have G6PD deficiency, unless already known *[see Warnings and Precautions, Contraindications]*.

Gout Flares

Explain to patients that gout flares may initially increase when starting treatment with KRYSTEXXA, and that medications to help reduce flares may need to be taken regularly for the first few months after KRYSTEXXA is started *[see Warnings and Precautions, Adverse Reactions]*. Advise patients that they should not stop KRYSTEXXA therapy if they have a flare.

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Adding Mineralocorticoid Receptor Antagonists to SGLT2 Inhibitors: Should We Push the Envelope?

By Micah Schub and Matthew A. Sparks

In recent years, the addition of sodium glucose co-transporter 2 (SGLT2) inhibitors to maximally tolerated renin-angiotensin system (RAS) blockade for the treatment of diabetic and non-diabetic proteinuric kidney disease has been a monumental development for the field of nephrology. Both the CREDENCE and DAPA-CKD trials showed a significant reduction in a composite kidney outcome (doubling of serum creatinine, progression to end stage kidney disease, and death from kidney or cardiovascular causes) and a reduction in albuminuria (1, 2). Similarly, in the recent FIDELIO-DKD and FIGARO-DKD trials, use of the non-steroidal mineralocorticoid receptor antagonist (MRA) finerenone showed a significant reduction in a composite kidney outcome and a reduction in albuminuria (3, 4). Post hoc analyses of these trials showed that the nephroprotective effects of both drug classes (SGLT2 inhibitors and MRAs) may be complementary, even in addition to RAS blockade. However, these analyses were post hoc and did not address albuminuria reduction. Moreover, questions remain whether traditional steroidal MRAs (spironolactone or eplerenone), which are less expensive, would provide the same benefit as non-steroidal MRAs (finerenone).

The Rotation for Optimal Targeting of Albuminuria and Treatment Evaluation (ROTATE)-3 study, recently published in *JASN* (5), randomized 46 patients, aged ≥18 years, with urinary albumin excretion ≥100 mg per 24 hours and ≤3500 mg per 24 hours; with an estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m^2 and <90 mL/min/1.73 m^2; with serum potassium ≤5 mmol/L; and who were on stable doses of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for more than 4 weeks. The study used three consecutive open-label crossover treatment periods of 4 weeks each, in which patients were treated with the MRA eplerenone 50 mg once daily, the SGLT2 inhibitor dapagliflozin 10 mg once daily, or a combination of eplerenone 50 mg once daily and dapagliflozin 10 mg once daily.

The primary outcome was change in the urinary albumin-to-creatinine ratio (UACR) from baseline between treatments. The baseline mean UACR in all participants was 401 mg/g. After 4 weeks of treatment, reduction in albuminuria was greatest in the combined dapagliflozin-eplerenone period (–53%), then the eplerenone period (–33.7%), followed by the dapagliflozin period (–19.6%). Interestingly, there was no association between individual UACR change during the individual dapagliflozin and eplerenone periods (r = 0.07; p = 0.63). There was a significant increase in potassium in the eplerenone period (+0.36 mmol/L), but this appeared to be blunted by addition of dapagliflozin in the dapagliflozin-eplerenone period (+0.23 mmol/L).

Persistent albuminuria and poor response to treatment are associated with risk of kidney disease progression and poor cardiovascular outcomes. The ROTATE-3 study suggests that the combination of SGLT2 inhibitors and MRA, in addition to maximal RAS blockade, is better at reducing albuminuria than either treatment alone. Importantly, patients showed a varied response to the different classes of medicines, indicating that patients who do not respond to one treatment may benefit from the other. Intriguingly, the addition of SGLT2 inhibitors to MRA therapy may reduce the incidence of hyperkalemia, potentially improving the safety profile of MRAs.

These findings support the need for large randomized controlled trials assessing clinical outcomes of these two medication classes in combination. Moreover, traditional steroidal MRAs can be considered until direct comparison studies are performed with the novel non-steroidal MRA finerenone, unless patients are not able to tolerate steroidal MRAs. The ROTATE-3 study sheds light on this important clinical conundrum. The next era of kidney disease treatment is coming into focus and appears to be triple therapy: RAS blocker, SGLT2 inhibitor, and MRA. ■

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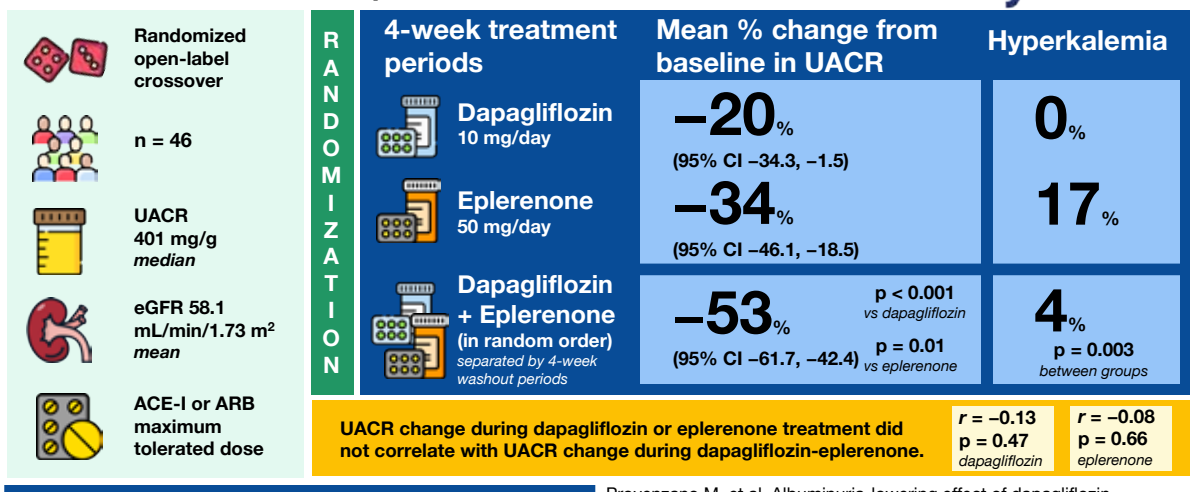
The authors report no conflicts of interest.

Albuminuria-lowering effect of dapagliflozin, eplerenone, and their combination in patients with CKD

KidneyNews



Conclusions: Albuminuria changes in response to dapagliflozin and eplerenone did not correlate, supporting systematic rotation of these therapies to optimize treatment. Combining dapagliflozin with eplerenone resulted in a robust, additive, UACR-lowering effect. CKD, chronic kidney disease.

Provenzano M, et al. Albuminuria-lowering effect of dapagliflozin, eplerenone, and their combination in patients with chronic kidney disease: A randomized crossover clinical trial. *JASN* 2022; 33:1569–1580. doi: 10.1681/ASN.2022020207

Visual Abstract by Edgar Lerma, MD, FASN

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Can Anakinra Reduce Inflammation in Hemodialysis?

By Latoya Gayle and Jeffrey Silberzweig

Inflammation is implicated in the pathogenesis of cardiovascular disease and protein-energy wasting, which are important contributors to morbidity and mortality of patients with end stage kidney disease. It has been postulated that suppressing inflammation with anti-cytokine therapy may improve inflammation and related outcomes.

ACTION, a parallel group, double-blind, randomized placebo-controlled pilot trial, evaluated the efficacy, safety, and tolerability of anakinra in hemodialysis patients (1). Eighty patients were randomized to receive anakinra or placebo via their hemodialysis circuit, three times weekly for 24 weeks and then followed for an additional 24 weeks. Highly sensitive C-reactive protein (hsCRP), interleukin (IL)-6, IL-10, IL-1β, tumor necrosis factor-α, and white cell count were collected pre-dialysis at two screening visits and at follow-up visits every 4 weeks (1). Anakinra was well tolerated, with similar adverse events in both arms. Notably, there were no infectious complications, despite the fact that anakinra can reduce the ability to control infections and can cause leukopenia. IL-6 levels decreased significantly in the treatment group with no change in the placebo arm. There was also a greater reduction in hsCRP in the anakinra group; however, the decrease was not statistically significant. Because of the short duration of the study, hard endpoints, such as cardiovascular events and changes in weight, were not examined. The ACTION trial suggests that the use of anakinra to reduce inflammation in patients treated by maintenance hemodialysis is safe, well tolerated, and feasible. The small study size and uniform age distribution limit generalizability of the results. None of the enrolled patients received dialysis via catheters, which may contribute to inflammation; thus, further study is necessary.

The findings of the ACTION trial provide a new outlook into the potential for treatment of inflammation with anti-cytokine therapy in patients receiving maintenance hemodialysis. Further study is needed to assess how these findings trans-

Extreme Prematurity and Kidney Outcomes: Should We Care?

By Tahagod Mohamed and Michelle Starr

Knowledge of the impact of extreme prematurity on long-term kidney outcomes is quickly evolving (1, 2). Several previous studies reported an association of extreme prematurity with worse kidney outcomes in children and adults (1–5). Kidney outcomes are particularly worrisome in children born at <28 weeks of gestation (often referred to as extremely low gestational age neonates or ELGANs) and in very low birthweight infants (<1500 g). These infants are likely to have the lowest nephron number due to premature birth and resulting incomplete and/or abnormal nephrogenesis (6). Previously studied kidney outcomes included abnormal kidney function, as evidenced by abnormal estimated glomerular filtration rate (eGFR), proteinuria, and hypertension. However, the onset of these findings is not fully characterized. There are currently no expert recommendations for when to initiate screening and evaluation for kidney diseases in former ELGANs. Some studies (4) suggest that chronic kidney disease (CKD) in former extremely preterm children can be detectable as early as school age. Other reports show evidence of CKD in adolescence (5) or later in life when former extremely preterm individuals are followed for several decades (2, 3).

Hingorani and colleagues (7) further explore this question using the Recombinant Erythropoietin for Protection of Infant Renal Disease (REPAIReD) cohort. REPAIReD evaluated kidney outcomes in ELGANs enrolled in the Preterm Erythropoietin Neuroprotection Trial (PENUT), a prospective multicenter study (8). Hingorani et al. (7) report the prevalence and risk factors of kidney diseases and hypertension at 2 years of age in former ELGANs. The study is unique in evaluating kidney outcomes at an early age in former ELGANS (n = 565). At 2 years old, more than one-half of participants (53%) had evidence of kidney diseases, including CKD, as evidenced by abnormal eGFR (18%), albuminuria (36%), and systolic (22%) and diastolic (44%) hypertension. Younger gestational age, smaller birthweight, and treatment with prenatal steroids were associated with increased risk of CKD. Factors that associated with increased risk of hypertension included male sex, Black race, treatment with indomethacin, and neonatal acute kidney injury.

These findings have implications for the kidney care of ELGANs. They provide insight into inpatient care and long-term follow-up of kidney health for former ELGANs. Robust patient education before discharge from the neonatal intensive care unit (NICU) about the risks of long-term kidney diseases and the need for monitoring can play a role in improving family awareness. Documentation of the risk of kidney diseases in patient health records is also important to promote regular blood pressure evaluation at each pediatrician visit. Follow-up with a nephrologist may be warranted for some children, especially those with a history of acute kidney injury or any other kidney-related complication (e.g., hypertension) during NICU admission. Research is needed to allow longitudinal follow-up of former ELGANs after graduation from the NICU to better define the natural course of prematurity-associated kidney diseases and the optimal timing for initiation and interval of follow-up and screening for kidney diseases in former ELGANs. ■

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The authors report no conflicts of interest.

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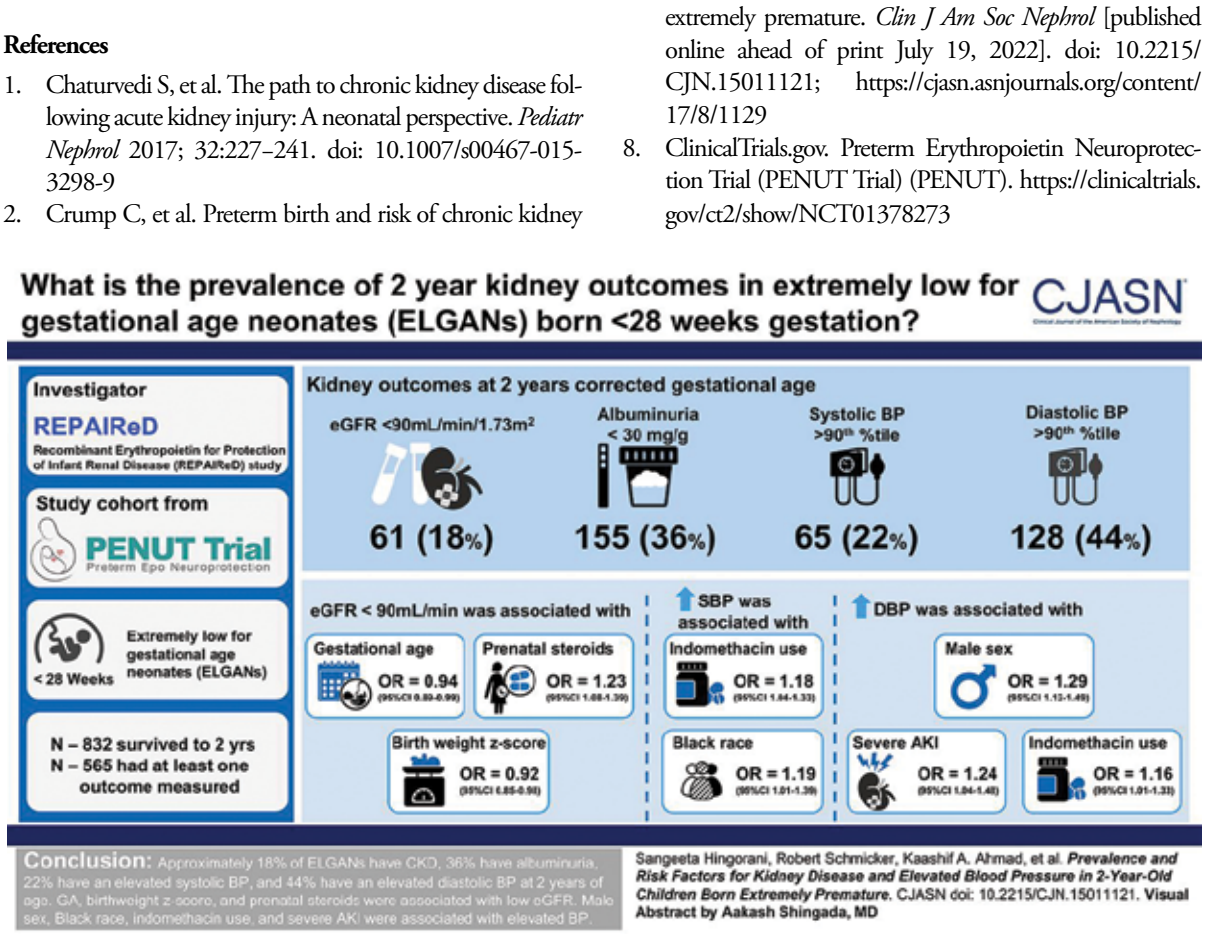

late into the clinical setting with expanded endpoints, including cardiovascular disease, infection, and protein energy wasting and their associated morbidity and mortality. ■

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Dr. Silberzweig is employed by The Rogosin Institute. He receives research funding from Kaneka Pharma America and receives consultative fees from Alkahest, Bayer, Honeywell, Kaneka Pharma America, and Saint-Gobain. He serves as co-chair of ASN's COVID-19 Response Team and Emergency Partnership Initiative. Dr. Gayle reports no conflicts of interest.

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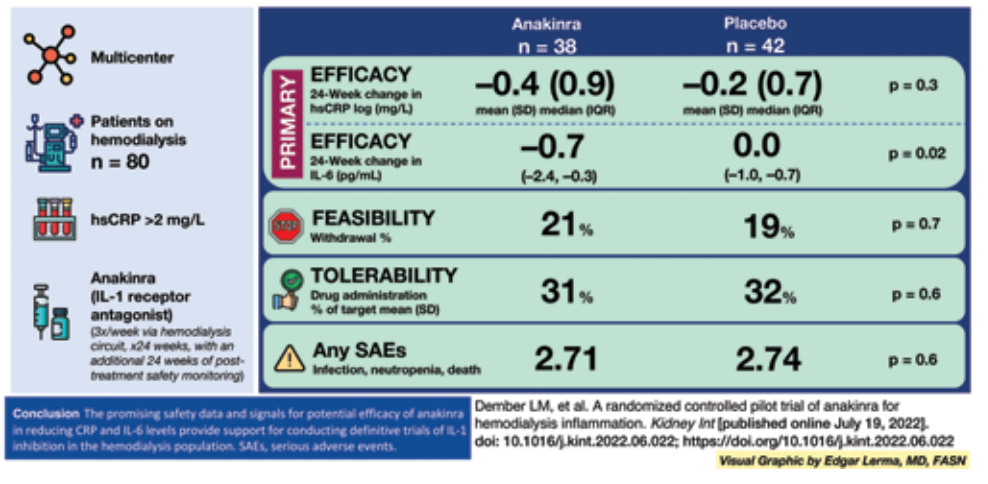
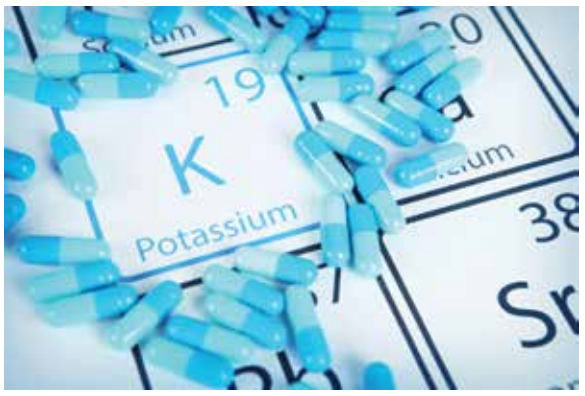


Potassium Supplementation in Chronic Kidney Disease

By Carmen Cajina and Vivek Bhalla

Cardiovascular disease represents the leading cause of mortality in chronic kidney disease (CKD), and higher odds of cardiovascular events are associated with lower dietary potassium intake in the general population (1). However, due to the intrinsic risk of hyperkalemia, the effects and applicability of supplementation in patients with CKD are poorly studied.



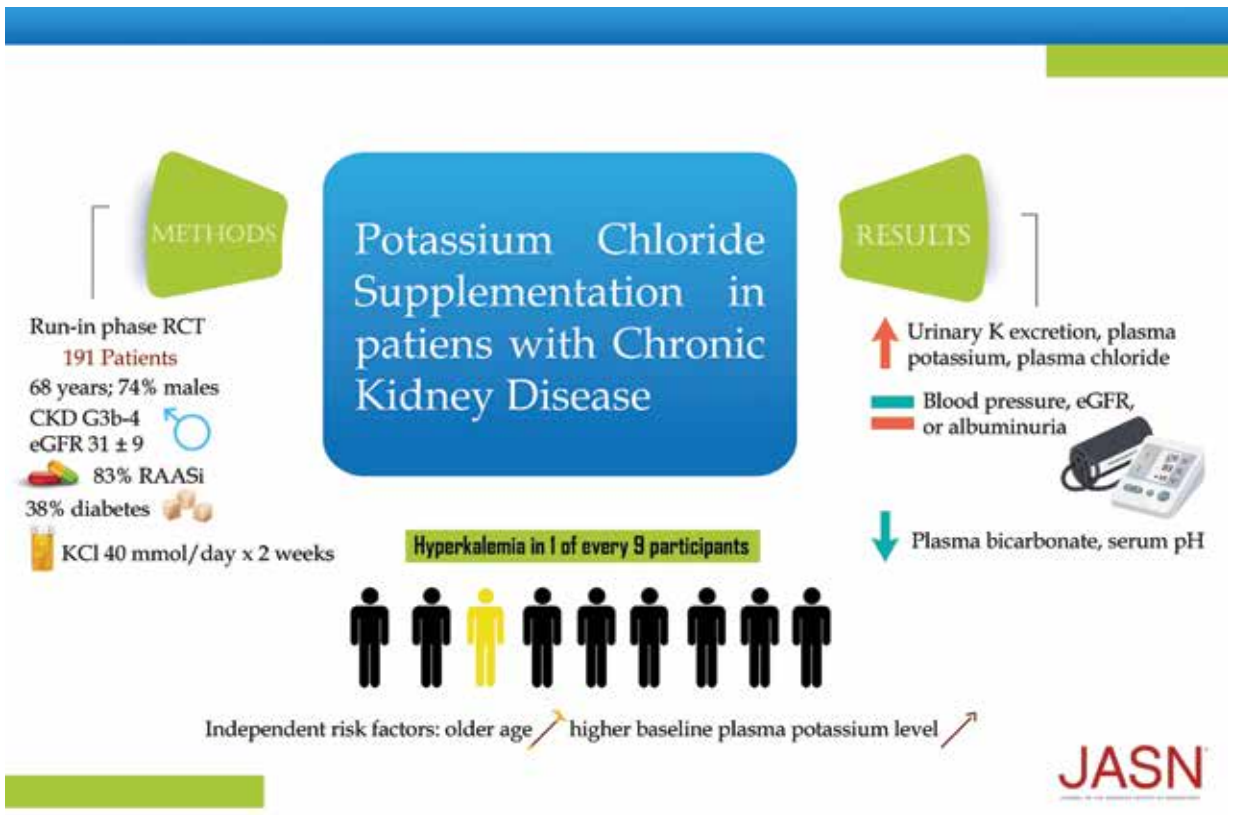
A new study was published in *JASN* (2) based on a prespecified analysis of an ongoing randomized controlled trial, which includes 191 patients with CKD stage G3b-4. Thirty-eight percent of patients have diabetes mellitus, and 83% were prescribed renin-angiotensin system inhibitors. During the run-in phase, patients received 40 mmol/day of potassium chloride for 2 weeks. This intervention resulted in the following: an increase in serum potassium of 0.4 mmol/L; no significant effect on blood pressure, estimated glomerular filtration rate, albuminuria, or urinary sodium excretion; and hyperkalemia (plasma potassium, 5.9 ± 0.4 mmol/L) in 21 participants (11%). Multivariable analysis demonstrated that older age and higher baseline plasma potassium were independently associated with the risk of hyperkalemia after supplementation.

In basic science studies, a primary mechanism by which high potassium intake reduces blood pressure is by lower phosphorylation or dephosphorylation of the sodium chloride co-transporter, located along the distal convoluted tubule (3, 4). The majority of mechanisms that are associated with dietary changes are ascribed to subsequent changes in the plasma potassium. On the other hand, studies have demonstrated a higher number of cardiovascular and kidney events with very low or very high serum potassium (5). Thus, it remains unclear if benefits of potassium supplementation, which are not accompanied by a rise in plasma potassium, would be beneficial overall.

Potassium supplementation comes in different forms. Importantly, this study will compare the effects between potassium chloride and potassium citrate in CKD. Specifically, the type of potassium salt may be critical to determine the risk:benefit ratio. Although potassium chloride reduces blood pressure and cardiovascular disease compared with sodium chloride (6), potassium citrate might lower blood pressure—and therefore, cardiovascular risk—more than potassium chloride (7–9). Moreover, fewer acidic therapies may ameliorate the anticipated hyperchloremic acidosis.

One potential adverse effect of a higher potassium diet on CKD progression is the accompanying rise in aldosterone secretion. Independent of changes in blood pressure, aldosterone levels directly correlate with CKD progression (10) and vascular disease (11). Moreover, mineralocorticoid receptor blockade in patients with diabetes reduces major cardiovascular and kidney events (12, 13). This concern prompts a significant question: Does potassium supplementation benefit patients despite the increase in aldosterone levels?

In conclusion, this prespecified analysis demonstrates the feasibility of the authors' intended, longer-term study, which is already an important step forward. Nevertheless, the high rate of hyperkalemia with more immediate and long-term sequelae must be weighed against potential beneficial outcomes of potassium chloride or potassium citrate.



eGFR, estimated glomerular filtration rate; KCl, potassium chloride; RAASi, renin-angiotensin-aldosterone system inhibitors; RCT, randomized control trial.

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Dr. Cajina reports no conflicts of interest. Dr. Bhalla has previously served on an advisory board for Relypsa.

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Jacqueline Emathinger, BS
Elucidating the Protective Role of Proximal Tubule ACE2 in Acute Kidney Injury

Yuting Zeng, MS*
Podocyte Inflammation Accelerates Parietal Epithelial Cell Injury in the Aged Kidney

** Kidney Week 2022 oral and/or poster abstract presenter*

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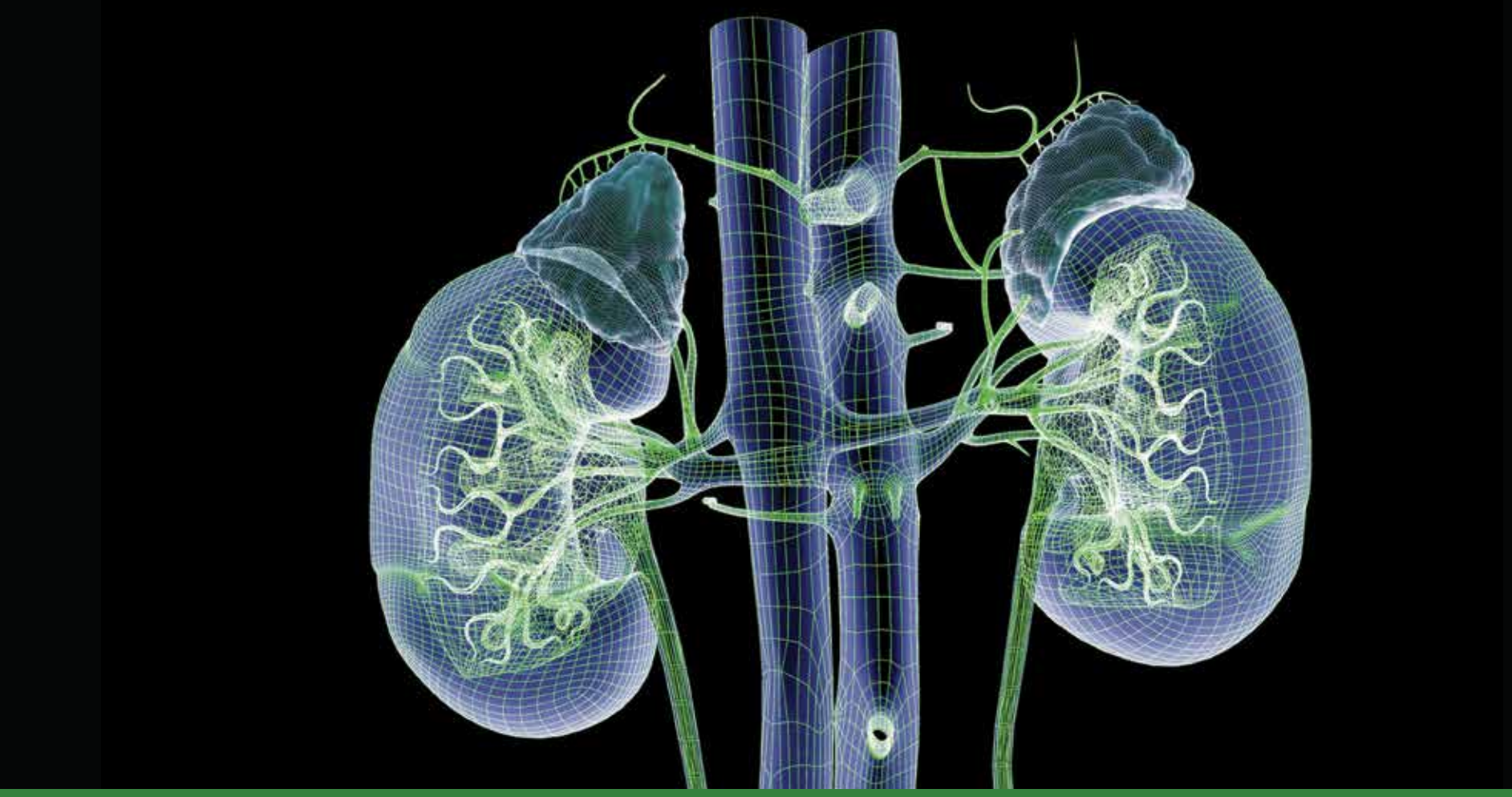

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Atrasentan (ALIGN)	IgA Nephropathy						Phase 3 ongoing
Atrasentan (AFFINITY)	Basket glomerular diseases					Phase 2 ongoing	
BION-1301	IgA Nephropathy					Phase 1/2 ongoing	
CHK-336	Primary Hyperoxaluria				Phase 1 HV study ongoing		
Research & Discovery Programs	Rare, severe chronic kidney diseases	Multiple programs at different stages					

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- BION-1301 is a novel anti-APRIL monoclonal antibody with a potentially disease-modifying approach to treating IgAN by reducing Gd-IgA1, the pathogenic IgA variant, demonstrated preclinically as well as clinically in both healthy volunteers and patients with IgAN.
- CHK-336 is an oral small molecule lactate dehydrogenase A inhibitor with liver-targeted tissue distribution in development for the treatment of patients with primary and idiopathic hyperoxaluria.

Atrasentan, BION-1301, and CHK-336 are investigational agents and have not been approved for any uses in patients.

The ALIGN study is a global, phase 3 clinical trial of atrasentan in patients with IgA nephropathy at high risk for progressive kidney function loss.

The study is currently enrolling patients.

TARGETED THERAPY

for IgA Nephropathy

Selective endothelin A (ET_A) blockade represents a potential approach to reduce proteinuria and preserve kidney function in high-risk IgAN patients.

Atrasentan:

- Is a potent and selective ET_A antagonist
- Has been studied extensively in over 5,000 diabetic nephropathy patients, consistently demonstrating rapid and sustained reductions in proteinuria
- Reduced the risk of major kidney events in a global Phase 3 outcome study in diabetic nephropathy (SONAR)

For more information, visit AlignStudy.com or ClinicalTrials.gov: NCT04573478

ALIGN

CHINOOK THERAPEUTICS

Atrasentan is an investigational agent and has not been approved for any uses, including in patients with IgA nephropathy.

Recent ASN Advocacy Efforts in Transplantation, Dental Coverage, and Medicare Quality and Health Equity

Summer 2022 ushered in a whirlwind of regulatory activities that herald an array of changes underway in kidney health care. These changes represent a range of advocacy efforts undertaken by ASN and other members of the kidney community over the past decade.

Kidney transplantation

In June 2022, ASN and the National Kidney Foundation (NKF) continued their work together following the December 2021 publication in *JASN* of A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease[s] (1), advocating with the Organ Procurement & Transplantation Network (OPTN) board of directors to pass a proposal to require transplant hospitals to use race-neutral calculations when estimating a patient's glomerular filtration rates for patients being considered for kidney transplantation. ASN and NKF also requested that the OPTN board address the use of race factors in the Kidney Donor Risk Index. On June 27, 2022, the OPTN board unanimously approved a measure to require transplant hospitals to use a race-neutral calculation when estimating a patient's level of kidney function (2).

Dental coverage for transplant candidates and recipients

Researchers have long demonstrated that "[O]ral health represents a potential determinant of health outcomes in patients with end-stage renal diseases (ESRD)." Studies show that adults with ESRD have more severe oral disease than the general population, which can lead to increased mortality. As a result, the Centers for Medicare & Medicaid Services (CMS) proposed that Medicare expand access to dental services for individuals seeking kidney transplant or receiving immunosuppressant medications in a physician fee schedule beginning in calendar year 2023.

ASN expressed its strong, ongoing support for this proposal in its comment letter to CMS, highlighting that access to dental services is important for dialysis patients as part of their ability to access kidney transplants, as well as being essential for accessing cardiovascular procedures for valvular disease, which is more common in dialysis patients. Specifically, ASN strongly encouraged CMS to finalize the following:

- Clarify that payment can be made under Medicare Part A and Part B for dental services that are inextricably linked to and substantially related and integral to the clinical success of an otherwise covered medical service, including dental or oral examination, as part of a comprehensive work-up before a kidney transplant surgery, as well as clarify that payment can be made for services that are ancillary to these dental services, such as X-rays, administration of anesthesia, use of an operating room, and other facility services, regardless of whether the services are furnished in an inpatient or outpatient setting.
- Expand payment under Medicare Parts A and B for dental services that are inextricably linked to and substantially related and integral to the clinical success of a certain covered medical service and are not subject to the exclusion under the Social Security Act, including the dental or oral examination, as part of a comprehensive work-up before an organ transplant, cardiac valve replacement,

or valvuloplasty procedure, and expand necessary dental treatments and diagnostics to eliminate oral or dental infections found during a dental or oral examination as part of a comprehensive work-up before an organ transplant, as well as for services that are ancillary to these dental services, such as X-rays, administration of anesthesia, and use of the operating room, regardless of whether the services are furnished in an inpatient or outpatient setting.

- Expand payment to include dental examinations and medically necessary diagnostic and treatment services before treatments that include initiation of immunosuppressant therapy.

Easing disparities and ensuring quality in the Medicare ESRD Program

CMS requested information on quality indicators for home dialysis in the proposed ESRD Prospective Payment System (PPS), Quality Incentive Program (QIP), and ESRD Treatment Choices (ETC) Model rule and highlighted the two general types of dialysis currently in use: hemodialysis (HD) and peritoneal dialysis (PD). CMS noted that although HD can be performed both in-center and at home (and PD can be furnished in both sites of care as well), for the purposes of the Request for Information (RFI) in the proposed rule, CMS considers PD to be exclusively a home modality.

Since 2020, the International Society for Peritoneal Dialysis has recommended that the adequacy of PD should no longer be determined by Kt/V (K, clearance; t, dialysis time; V, volume of distribution). Rather, home dialysis should be "goal directed" to promote high-quality dialysis care that helps patients meet their own individual care goals (e.g., remaining independent at home and maintaining a high quality of life). Given current treatment guidelines, an over-reliance on Kt/V as a quality measure for PD runs counter to the spirit of patient-reported outcome measures and thus, may encroach on patient-centered care.

ASN recommended that CMS reevaluate the assessment of Kt/V in PD by examining and tailoring the performance

Continued on page 38

Recent ASN Advocacy Efforts

Continued from page 37

standards within the ESRD QIP separately for in-center HD and PD. Currently, the PD and HD performance standards for achievement threshold, median, and benchmark Kt/V in dialysis are the same regardless of modality, with a median performance standard of 97.61% estimated for program year 2025 (with an achievement threshold of 94.33% and benchmark of 99.42%). These standards are inappropriate for a substantial proportion of PD patients, as discussed in the current PD guidelines. ASN believes that achieving a target Kt/V should be disaggregated for PD and HD, with the application of different performance standards for PD. These can then be reaggregated at the facility level to comprise a revised Kt/V comprehensive measure that does not disadvantage patients electing for PD and facilities providing PD.

ASN urged CMS to convene a technical expert panel to evaluate the basic framework for these performance standards through the lens of clinical knowledge and intended to limit unintended consequences and individualize care, realizing that the proportion of patients at a facility who achieve a given Kt/V threshold for in-center HD typically will be higher than the proportion for PD. ASN also recommended prioritization of outcome measures to focus on relevant clinical outcomes, such as reporting peritonitis rate as the number of episodes per patient year, inpatient readmission rates, and mortality. Other types of metrics that ASN recommended that CMS review were patient-reported outcome measures and patient-reported experience measures as key home dialysis indicators.

CMS also asked an array of questions in the proposed rule in a section titled "Requesting comments on improving CMS's ability to detect and reduce health disparities for individuals receiving renal dialysis services."

ASN recommended CMS consider a health equity incentive model, similar to the ETC Model, with a similarly structured incentive in which a payment adjustment is based on the percentage of patients who are dual eligible or with a low-income subsidy (to incentivize care of these patients). The model could include add-on payments for a higher percentage of dual-eligible home dialysis patients or patients with social challenges, such as housing and/or food insecurity. In response to the RFI, ASN discussed a number of comorbidities that should be examined when calculating case-mix adjustors, such as mental health diagnoses (e.g., depression related, bipolar disorder, anxiety, and substance abuse), language and communication barriers, physical disabilities (i.e., wheelchair dependency), and social determinants of health, including but not limited to housing and food insecurity.

ASN further endorsed accurate and standardized, self-identified demographic information (including information on race and ethnicity, disability, sexual orientation, gender identity, socioeconomic status, geography, and language preference) for the purposes of reporting, stratifying data by population, and other data collection efforts that CMS believes would refine the ESRD PPS payment policy.

ASN also discussed the use of Z codes (used as reason codes to capture factors that influence health status and contact with health services) and how suppression of data from certain quality measures in the QIP would affect the rating results in 2023, as those ratings are based on data from 2021 and were heavily impacted by COVID-19. ■

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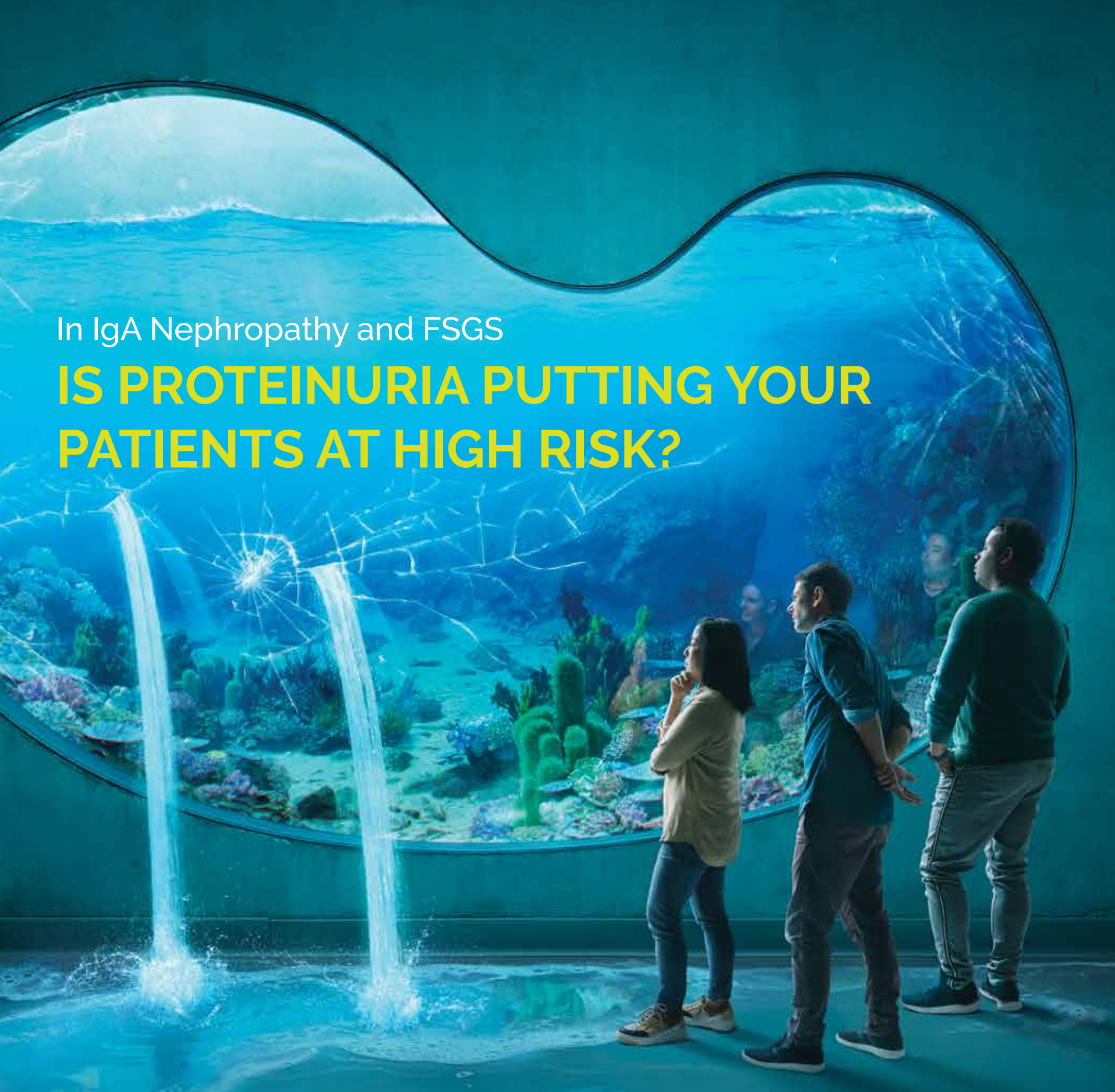
In IgA Nephropathy and FSGS

IS PROTEINURIA PUTTING YOUR PATIENTS AT HIGH RISK?



Elevated proteinuria is a marker of increased risk of disease progression in patients with IgA Nephropathy and FSGS[1]

Learn more at **LowerProteinuria.com**

IgA nephropathy=immunoglobulin A nephropathy;
FSGS=focal segmental glomerulosclerosis.

References: 1. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int 2021: 100(4S):S1-S276.

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As of September 1, 2022

PLENARY SESSION

Kidney Week to Open with Panel on Pandemic Prevention

Peter J. Hotez, MD, PhD

Carlos del Rio, MD

ASN is partnering with the National Academy of Medicine to kick off Kidney Week with a special opening plenary on Thursday, November 3, on countering the threat of future pandemics.

An internationally recognized expert on neglected tropical diseases and vaccine development will present the keynote address on "Preventing the Next Pandemic." The speaker will be Peter J. Hotez, MD, PhD, dean of the National School of Tropical Medicine and professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine in Houston, TX.

Dr. Hotez is also the co-director of the Texas Children's Hospital Center for Vaccine Development, where he leads a team aimed at developing new vaccines for hookworm infection, schistosomiasis, leishmaniasis, Chagas disease, and SARS/MERS/SARS-CoV-2 coronavirus diseases that affect hundreds of millions of children and adults worldwide. A champion of access to vaccines globally and in the United States, last year, he published the book, *Preventing the Next Pandemic: Vaccine Diplomacy in a Time of Anti-science*.

The keynote will be followed by an expert panel moderated by Carlos del Rio, MD, who is a distinguished professor of medicine in the Division of Infectious Diseases at the Emory University School of Medicine in Atlanta, GA; co-director of the Emory Center for AIDS Research; and co-principal investigator of the Emory–Centers for Disease Control and Prevention HIV Clinical Trials Unit.

Dr. del Rio has been a local and national leader during the COVID-19 pandemic, conducting research, developing policies, writing scientific publications, and making media appearances. His research focuses on early diagnosis, access to care, compliance with anti-retrovirals, and prevention of HIV infection. He has worked for over a decade with hard-to-reach populations to improve outcomes related to HIV.

They will be joined on the panel by three other experts:

Timothy G. Evans, MD, PhD

Jennifer B. Nuzzo, DrPH

Reed V. Tuckson, MD

- Timothy G. Evans, MD, PhD, is associate dean of the School of Population and Global Health at McGill University. He was named executive director of Canada's COVID-19 Immunity Task Force in April 2020. Dr. Evans has been at the forefront of advancing global health equity and strengthening health delivery for more than 20 years. From 2003 to 2010, he was assistant director general at the World Health Organization, where he led the Commission on Social Determinants of Health and oversaw production of the annual World Health Report. He has co-founded many partnerships, including the Global Alliance on Vaccines and Immunization. His previous positions include serving as dean of the James P. Grant School of Public Health at BRAC University in Dhaka, Bangladesh.
- Jennifer B. Nuzzo, DrPH, is professor of epidemiology and director of the pandemic center at the Brown University School of Public Health. She is also a senior fellow for global health at the Council on Foreign Relations. Her work focuses on global health security, public health preparedness and response, and health systems resilience. With colleagues from the Nuclear Threat Initiative and the Economist Intelligence Unit, she co-leads the development of the first ever Global Health Security Index, which rates 195 countries' public health capabilities; commitment to international norms; and socioeconomic, political, and environmental risk environments. Dr. Nuzzo also directs the Outbreak Observatory, which conducts research to improve outbreak preparedness and response. She regularly advises national governments, companies, and nonprofit organizations on pandemic preparedness and response.
- Reed V. Tuckson, MD, is managing director of Tuckson Health Connections, a vehicle to advance initiatives that support optimal health and well-being through health promotion and disease prevention, applied data and analytics, enhanced quality and efficiency in care delivery, and the application of telehealth and biotech innovations. He is a co-founder of the Black Coalition Against COVID, an interdisciplinary effort working to mitigate the COVID-19 pandemic in Washington, D.C., and nationally. He served for many years as executive vice president and chief of medical affairs for UnitedHealth Group, a Fortune 20 company. Dr. Tuckson has been appointed to leadership roles at the National Institutes of Health, National Academy of Medicine, and other federal advisory committees, as well as several corporate, nonprofit, and academic boards.

Winn Lecturer to Speak on Virus and Genome Rescue

Moin Saleem, MBBS, MBChB, MD, PhD

A gene therapy researcher will describe "Adeno-Associated Virus (AAV) Genome Rescue of *NPHS2* in Mice" in the Michelle P. Winn, MD, Endowed Lectureship on Thursday, November 3.

Moin Saleem, MBBS, MBChB, MD, PhD, heads Bristol Renal, a glomerular research group of approximately 45 researchers that encompasses many areas, including cell biology, transgenic models, and population cohorts and genetics. He is also a professor of pediatric renal medicine at the University of Bristol in the United Kingdom.

Dr. Saleem has published extensively about adeno-associated virus gene therapy to prevent progression of kidney diseases in genetic human and mouse models of nephrotic syndrome. Gene therapy targeting the kidney has proven challenging, although AAV has been used successfully for gene therapy targeting other organs, with particular success in targeting monogenic diseases.

The most common cause of genetic nephrotic syndrome in children is a mutation in the *NPHS2* gene encoding podocin. Among other approaches, Dr. Saleem and colleagues have tested AAV-mediated gene therapy in a conditional podocin knockout mouse model and in human podocytes with the most common podocin mutation.

Dr. Saleem was the originator of the UK Registry of Rare Kidney Diseases and currently leads the UK National Study of Nephrotic Syndrome (NephroS) and a major industry-academic collaboration, termed NURTuRE (National Unified Renal Translational Research Enterprise). NURTuRE is a national cohort and biobank of patients with chronic kidney disease and nephrotic syndrome who are being studied for stratification and re-definition of diseases, according to molecular phenotypes. This effort is being extended to international cohorts in developing countries. Dr. Saleem's work in genetic stratification of nephrotic syndromes has led to gene discoveries and the establishment of national clinical gene panels that have been integrated into new international testing guidelines.

His laboratory undertakes research from basic cell and animal biology and physiology to studies of international patient cohorts with rare diseases, including genome sequencing and systems biology approaches. The lab has developed the world's gold standard glomerular cell lines. He commenced his gene therapy program in 2014 and is a founder of the field of podocyte biology with a focus on targeting the podocyte to radically change the treatment of kidney diseases. He is the co-founder and chief scientific officer of Purespring Therapeutics, the world's first renal gene therapy biotech company featuring research programs for diseases with no currently effective therapies. Dr. Saleem received a PhD in transplantation immunology from the Institute of Child Health in London. He trained in pediatric nephrology at the Great Ormond Street Hospital in London.

Transplant Expert Will Share Lessons on Kidney Graft Success

Roslyn B. Mannon, MD, FASN

A former president of the American Society of Transplantation will relate her experiences from a long career in the Barbara T. Murphy, MB BAO BCh, FRCPI, Endowed Lectureship. Roslyn B. Mannon, MD, FASN, will address "Improving Kidney Graft Long-Term Outcomes: Lessons Learned and New Perspectives" on Thursday, November 3.

Dr. Mannon is professor of medicine, pathology, and microbiology; vice chair for academic development and research mentoring; and associate chief of nephrology for research at the University of Nebraska Medical Center.

Her research focuses on mechanisms of chronic graft injury using in vitro and rodent models and is funded by the Veterans Administration Merit Award. She has contributed approximately 200 peer-reviewed publications on the mechanisms of chronic allograft failure following transplantation, posttransplant complications, and immune monitoring. She began her career as a staff physician at the Durham VA Medical Center and assistant professor of medicine at Duke University Medical Center. She spent several years as medical director for the Kidney/Pancreas Intramural Transplant Program of the National Institute of Diabetes and Digestive and Kidney Diseases and more than a decade at the University of Alabama at Birmingham, where she was section chief of transplant nephrology in addition to serving at the Birmingham VA Medical Center.

Dr. Mannon is deputy editor of the *American Journal of Transplantation*. She chairs The Transplantation Society initiative Women in Transplantation and the ASN Policy and Advocacy Committee and co-chairs the Scientific Registry of Transplant Recipients Review Committee. Among many honors, she received the Young Investigator Award from the American Society of Transplant Physicians and volunteer service awards from the National Kidney Foundation of the National Capital Area.

Dr. Mannon received an MD from Duke University and completed an internal medicine internship and nephrology fellowship at Duke, where she also served as chief resident.

Goal-Directed Therapies to Be Focus of Eknoyan Lecture

Katherine R. Tuttle, MD, FASN

Katherine R. Tuttle, MD, FASN, will present the Garabed Eknoyan, MD, Endowed Lectureship on Thursday, November 3, on "Implementing Goal-Directed Medical Therapies for Diabetic Kidney Disease."

Dr. Tuttle is executive director for research at Providence Health Care in Spokane, WA; co-principal investigator at the Institute of Translational Health Sciences; and professor of medicine at the University of Washington. Her major research interests are clinical and translational science and precision medicine strategies to tackle diabetic kidney disease, chronic kidney disease, diabetes, and hypertension. She has published more than 300 original articles and served as associate editor of *CJASN, American Journal of Kidney Diseases,* and *Clinical Decision Support in Medicine: Nephrology* and *Hypertension*. She has also served on the editorial boards of *Advances in Chronic Kidney Disease* and *American Journal of Nephrology*, as well as on advisory boards of *The Lancet Diabetes & Endocrinology* and *Nature Reviews Nephrology*.

Among her many honors are the Medal of Excellence from the American Association of Kidney Patients, the Garabed Eknoyan Award from the National Kidney Foundation, the YWCA Women of Achievement Award in Science, and two outstanding clinical faculty awards from the University of Washington.

Dr. Tuttle currently chairs the ASN Diabetic Kidney Disease Collaborative Task Force. She served on the inaugural Board of Directors of the Kidney Health Initiative and has chaired numerous other working groups and committees for organizations, including the National Institute of Diabetes and Digestive and Kidney Diseases, National Kidney Foundation, International Society of Nephrology, and American Diabetes Association.

She earned her medical degree and completed her residency in internal medicine at Northwestern University. She was a fellow in metabolism and endocrinology at Washington University in St. Louis and then completed her nephrology fellowship at the University of Texas Health Science Center in San Antonio.

Schrier Lectureship to Focus on Tools for Understanding AKI

Lloyd G. Cantley, MD, FASN

The Robert W. Schrier, MD, Endowed Lectureship will focus on "Integrating Analysis of Animal Models and Human Biopsies to Better Understand AKI" on Thursday, November 3. The speaker will be Lloyd G. Cantley, MD, FASN, C.N.H. Long Professor of Medicine, professor of cellular and molecular physiology, head of the Nephrology Training Program, and co-director of the Yale Center for Clinical Investigation at Yale University.

Dr. Cantley's research focuses on growth factor signaling and cellular response pathways involved in kidney injury and repair. His laboratory uses in vitro and in vivo model systems to unravel the intracellular signaling pathways that regulate the mechanisms of tubule formation and repair. These studies have provided experimental proof that scaffolding proteins can direct signaling proteins to sites in the cell to regulate cell shape and movement.

Dr. Cantley's laboratory continued the studies to define how these in vitro signals are expressed and regulated in vivo. His group identified a key role for bone marrow-derived cells in normal kidney repair and showed that this effect is due, in large part, to factors produced by trafficking macrophages. The team used proteomics to identify several of these secreted factors and to determine that they originate from alternatively activated macrophages. The researchers have found that there is a phenotypic switch from proinflammatory to alternatively activated macrophages following kidney injury, and the alternatively activated cells are critical for tubule cell proliferation and repair.

In recent years, their work has shown that injured tubular cells themselves induce this alternative activation switch using regional expression of the granulocyte-macrophage colony-stimulating factor (GM-CSF), which induces a unique reparative macrophage activation profile for the repair response.

Among his many honors, Dr. Cantley has received a Physician-Scientist Award from the National Institutes of Health and the Joseph E. Murray Award from the National Kidney Foundation. He has chaired many sessions at ASN meetings and served as associate editor of *JASN*.

Dr. Cantley attended medical school at West Virginia University, followed by internal medicine training at the University of North Carolina and a nephrology fellowship at Beth Israel Hospital and Harvard Medical School in Boston. He was on the faculty at Beth Israel until moving to Yale University in 2000.

PLENARY SESSION

STATE-OF-THE-ART LECTURE

Lecture Will Focus on First Pig-to-Human Kidney Transplant

Jayme E. Locke, MD, MPH

A leading transplant surgeon will present a state-of-the-art lecture on "Making the Impossible Possible: First-in-Human Clinical Grade Kidney Xenotransplant" on Friday, November 4.

The speaker will be Jayme E. Locke, MD, MPH, who is professor of surgery and the Arnold G. Diethelm, MD, Endowed Chair in Transplantation Surgery at the University of Alabama at Birmingham (UAB). She is also director of the Comprehensive Transplant Institute and chief of the Division of Abdominal Transplant Surgery.

In September 2021, Dr. Locke's team performed a first-of-its-kind transplant, placing two genetically modified pig kidneys into a brain-dead human after removing the recipient's native kidneys. The transplanted kidneys filtered blood and produced urine. The kidneys were not rejected and remained viable for the 74-hour length of the experiment with no transmission of porcine retroviruses detected. The researchers first published their study on January 20, 2022, which appeared in the April edition of the *American Journal of Transplantation*.

Dr. Locke specializes in innovative strategies for the transplantation of incompatible organs, disparities in access to and outcomes after organ transplantation, and transplantation in HIV-infected end-stage patients. She is the surgical director of the South's leading incompatible kidney transplant program and coordinator of the UAB kidney chain, which is the longest living kidney-transplant chain in the United States, with 126 donors and recipients. Only the University of California, San Francisco, has performed more kidney transplants than UAB since statistics began being kept in 1988. UAB has performed 9055 kidney transplants, according to the United Network for Organ Sharing, including almost 3435 living donor transplants.

Dr. Locke's research interests include complex statistical analyses and modeling of transplant outcomes and behavioral research focused on health disparities. She has authored more than 140 articles in peer-reviewed journals and 20 book chapters. She is a deputy editor of the *American Journal of Transplantation* and is an editorial board member of the *Annals of Surgery*.

She has received many honors, including a distinguished investigator award from the Association for Clinical and Translational Science and a clinical investigator award from the American Society of Transplantation.

Dr. Locke received her medical degree from the East Carolina University Brody School of Medicine before training in general surgery and multi-visceral abdominal transplantation at The Johns Hopkins Hospital. She also received a Master of Public Health degree with an emphasis in biostatistics and epidemiology from the Johns Hopkins Bloomberg School of Public Health.

Three Patient Advocates Will Receive President's Medals

Glenda V. Roberts

Patrick O. Gee, Sr., PhD

David Rush

Three individuals living with kidney disease embodying diverse experiences will receive the ASN President's Medal during Kidney Week's Opening Plenary on Friday, November 4. The three recipients will be Glenda V. Roberts; Patrick O. Gee, Sr., PhD; and David Rush.

ASN presents the medal to individuals who have helped advance the society's mission to lead the fight against kidney diseases by educating health professionals, sharing new knowledge, advancing research, and advocating the highest quality care for patients.

Ms. Roberts is an individual living with long-term kidney disease who is director of external relations and patient engagement at the Center for Dialysis Innovation and the Kidney Research Institute at the University of Washington, Seattle. Before joining the university, Ms. Roberts spent 35 years as an information technology executive.

Based on her personal experience with kidney disease, Ms. Roberts is a passionate activist for kidney research and patients living with kidney disease. She managed the progression of her disease with diet and exercise for more than 40 years before undergoing dialysis. Since receiving a kidney transplant in 2010, she has completed nine half-marathons.

Ms. Roberts serves on myriad patient and community advisory committees, brings the patient voice to a number of National Institutes of Health and industry research efforts, and was one of two patients who were part of the National Kidney Foundation-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases.

Dr. Gee is the founder and chief executive hope dealer at iAdvocate, a nonprofit, faith-based health and wellness organization. He is also an ordained minister at Mountain Movers Ministry in Richmond, VA. He retired from his position as chief of security at the Virginia Department of Corrections in 2008.

Dr. Gee's kidney failure from diabetic kidney disease was treated with peritoneal hemodialysis until he received a transplant in 2017, which took more than 2 years to function normally. He uses his personal experiences to teach, coach, mentor, and educate others on how best to manage their outcomes.

To this end, he serves as a patient representative for the Diabetic Kidney Disease Collaborative Task Force; as vice chair of the Patient and Family Partnership Council of the Kidney Health Initiative; on advisory boards of Home Dialyzors United, the Center for Dialysis Innovation, and Patient & Family Centered Care Partners; and on U.S. Food and Drug Administration and National Institute of Diabetes and Digestive and Kidney Diseases committees on diversity, inclusion, and outreach.

He is also presenting the Celeste Castillo Lee Memorial Lectureship on "Incorporating Mental Health Practices by Increasing Psychosocial Education for Kidney Recipients" on Friday, November 4.

Mr. Rush is a platinum-selling recording artist. His battle with kidney disease began in high school, and he has been an in-center dialysis patient, home dialysis patient, and transplant recipient for 7 years until his body rejected the transplant. In 2009, he took his home hemodialysis machine on a 40-city world tour in which he was the opening act for multi-platinum rapper Pitbull.

Currently a home dialysis patient, he is a motivational speaker, patient/doctor consultant, and kidney care advocate at WinsOnly Lifestyle, LLC.

Mr. Rush has served for the past 5 years on the executive committee of the Northwestern University George M. O'Brien Kidney Research Core Center (NU GoKidney). He consults for major companies, such as AstraZeneca and Outset Medical, while still making waves in the world of entertainment as a writer and producer.

Ingelfinger to Be Presented Barbara T. Murphy Award

Julie R. Ingelfinger, MD

ASN will present the Barbara T. Murphy Award to Julie R. Ingelfinger, MD, on Friday, November 4. This is just the second year for this award, which is named for a nephrology leader who lost her battle with glioblastoma last year when she was ASN president-elect. The award honors leaders who strengthen the foundation of nephrology while advancing the field through innovation, creativity, inspiration, and tenacity.

Dr. Ingelfinger is professor of pediatrics at Harvard Medical School and senior consultant in pediatric nephrology at Mass General for Children at the Massachusetts General Hospital.

Her most prominent role is perhaps as deputy editor of *The New England Journal of Medicine* (*NEJM*), a position she has held since 2001. She teaches courses at *NEJM*—the world's highest-impact journal—and mentors authors year-round on a one-to-one basis.

Dr. Ingelfinger has been studying the intrarenal renin angiotensin aldosterone system for many years. Her other current projects focus on the role of maternal nutrition and maternal diabetes in renal development and perinatal programming. She is also investigating the role of maternal nutrition in renal development and the subsequent development of hypertension and mechanisms of proximal tubule injury.

She authored a text on pediatric hypertension and was an editor of the textbooks *Current Pediatric Therapy* and *Pediatric Hypertension*.

Among her many honors, Dr. Ingelfinger received the Dr. Donald N. Medearis Teaching Award from Massachusetts General Hospital, the Henry L. Barnett Award from the American Academy of Pediatrics, the Founders' Award from the American Society of Pediatric Nephrology, and the Honors Award from the National Kidney Foundation.

Dr. Ingelfinger received her MD from the Albert Einstein College of Medicine in New York City, followed by an internship in pediatrics at the Bronx Municipal Hospital Center. She completed residencies and fellowships in pediatrics and pediatric nephrology at St. Louis Children's Hospital, followed by further pediatrics training at St. Joseph's Hospital and Medical Center in Phoenix, Arizona.

Dr. Ingelfinger has spent her career at Harvard University, where she was appointed assistant professor in 1982, associate professor in 1988, and professor of pediatrics in 1999. She was chief of pediatric nephrology at Massachusetts General Hospital for 8 years.

John P. Peters Award to Honor Sharon Anderson

Sharon Anderson, MD, FASN

ASN will recognize the wide-ranging contributions of Sharon Anderson, MD, FASN, with the presentation of the John P. Peters Award on Friday, November 4. This award is given for outstanding contributions to improving the lives of patients and furthering the understanding of the kidney in health and diseases. Dr. Anderson has made these contributions as a clinician, educator, and researcher.

Dr. Anderson is professor of medicine in the Division of Nephrology and Hypertension at Oregon Health & Science University (OHSU) and a staff physician in the Nephrology Section at the Portland VA Medical Center. She also chairs the OHSU Department of Medicine and the OHSU Practice Plan. She served as chief of medicine at the Portland VA for 6 years and as executive vice president and dean of the OHSU School of Medicine for 4 years.

Dr. Anderson's research has focused on the progression of chronic kidney disease, with an emphasis on sex differences in kidney diseases, pathophysiology of the aging kidney, polycystic kidney disease, and diabetic nephropathy. She has been funded by the National Institutes of Health (NIH) and other granting agencies for many years and has more than 150 publications.

As an educator, she directed the Renal Fellowship Program at OHSU for many years and won numerous teaching awards.

Dr. Anderson also participates in myriad national activities. She was the first woman elected to the ASN Council, the first woman to serve as ASN president, and the first woman to chair the Nephrology Board of the American Board of Internal Medicine. She chaired the NIH General Medicine and the Pathobiology of Kidney Disease study sections and was a member of the National Institute of Diabetes and Digestive and Kidney Diseases Advisory Council and the NIH Council of Councils.

Among her many honors, she received the David M. Hume Memorial Award from the National Kidney Foundation and is a fellow of ASN and the American Heart Association.

Dr. Anderson received her medical degree from Louisiana State University Medical Center. After internal medicine residency training at OHSU, she completed her clinical fellowship in nephrology at the Beth Israel Deaconess Medical Center and her research fellowship at the Brigham and Women's Hospital of Harvard Medical School. After several years on the faculty there, she joined the faculty at OHSU and the Portland VA Medical Center in 1991.

Young Investigator Jennifer Pluznick Recognized for Understanding of Renal Receptors

Jennifer L. Pluznick, PhD

The ASN-American Heart Association Donald W. Seldin Young Investigator Award will be presented to Jennifer L. Pluznick, PhD, who will speak on "Unexpected Roles for Renal Olfactory Receptors," on Friday, November 4.

Dr. Pluznick is associate professor of physiology at the Johns Hopkins University School of Medicine.

She has made paradigm-shifting discoveries about renal physiology. As a postdoctoral fellow at Yale University 10 years ago, Dr. Pluznick reported the startling discoveries that olfactory receptors and companion olfactory signaling proteins are present in the kidney and modulate renal functions in important ways. Previously, it had been assumed that these receptors exclusively functioned in the nose. Dr. Pluznick's discoveries ignited a flurry of research that revealed "sensory" receptors have widespread roles in regulating the physiological functions of many non-sensory organs and tissues.

Since her seminal discovery, Dr. Pluznick has continued to break new ground in identifying novel functional roles for smell receptors. Her collaborative studies in the lung provided a proof of concept that olfactory receptors can be targeted to treat airflow obstruction in asthma.

Dr. Pluznick's receptor-signaling research field led to another discovery of broad fundamental significance: a mechanism to explain how gut microbiota influence host physiology. She discovered that certain smell receptors are activated by compounds that are exclusively produced by gut bacteria, and the activated receptors modulate host body functions.

Dr. Pluznick discovered that gut microbiota metabolites modulate the release of renin and thus influence blood pressure through activation of olfactory chemosensors in the kidney. Further studies confirming and expanding this finding introduced a new concept that changes in gut bacteria may drive salt sensitivity and hypertension. These studies suggest that altering gut bacteria might provide a means to lower blood pressure in hypertensive patients.

She has served on the ASN Kidney Week Program Committee.

Dr. Pluznick received her doctorate in renal physiology from the University of Nebraska Medical Center in Omaha, and then spent 5 years as a postdoctoral fellow at Yale University, where she studied both renal physiology and sensory systems with a specialty in olfaction. She joined the faculty at Johns Hopkins School of Medicine in 2010.

Rose Lectureship Will Focus on Managing Fluids in Septic AKI

Kathleen D. Liu, MD, PhD, FASN

The Burton D. Rose, MD, Endowed Lectureship will address "Fluid Management in Septic AKI: When, What Type, and How Much?" and will be held on Friday, November 4.

The speaker will be Kathleen D. Liu, MD, PhD, FASN, professor of medicine and anesthesia in the Divisions of Nephrology and Critical Care Medicine at the University of California San Francisco (UCSF), where she is also the medical director of the Medical Intensive Care Unit and the Apheresis/Hemodialysis Unit.

Dr. Liu's research has focused on acute kidney injury (AKI), acute respiratory distress syndrome, and critical care nephrology, with an emphasis on clinical trials. Currently, her main focus is on the predictive and pathogenetic role of biomarkers for both acute and chronic diseases with a long-term goal of identifying novel biomarkers of organ injury that may have predictive value for outcomes, as well as provide insight into disease pathogenesis. She also has a major interest in clinical trials in the intensive care unit, with a particular interest in acute lung injury and AKI.

Dr. Liu is a member of the National Institutes of Health Clinical Trials Network for the Prevention and Early Treatment of Acute Lung Injury and is involved in a US Department of Defense-funded clinical trial of mesenchymal stem cells for the treatment of trauma-associated acute respiratory distress syndrome. Her currently funded AKI research focuses on risk factors for AKI in collaboration with Kaiser Permanente of Northern California and on the pathways that mediate the relationship between AKI and subsequent cardiovascular disease in patients enrolled in the Assessment, Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury (ASSESS-AKI) study sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases.

Her service to professional organizations includes serving as a Steering Committee member of the ASN AKINow Initiative, as co-chair of a work group for the Kidney Disease: Improving Global Outcomes (KDIGO) AKI clinical practice guidelines, and as a member of the National Kidney Foundation Scientific Advisory Board. The Chinese American Society of Nephrology Young Investigator Award and an ASN Distinguished Leader Midcareer Award are among several awards that she has received.

Dr. Liu completed an MD/PhD program at UCSF. She then trained in internal medicine at Brigham and Women's Hospital in Boston and in nephrology and critical care at UCSF. She joined the UCSF faculty in 2006, where she has been since.

Lecture Will Address CKD-MBD Management

Eleanor D. Lederer, MD, FASN

A long-time researcher regarding chronic kidney disease-mineral bone disorder (CKD-MBD) will present a "Systems Biology Approach to Management of CKD-MBD" in the Jack W. Coburn, MD, Endowed Lectureship on Friday, November 4.

The speaker will be Eleanor D. Lederer, MD, FASN, who is the John S. Fordtran Professor of Medicine in Calcium Research at the University of Texas Southwestern Medical Center's Charles and Jane Pak Center for Mineral Metabolism and Clinical Research, co-director of the Dallas VA Network of Dedicated Enrollment Sites (NODES) program, and assistant chief of medical services at the VA North Texas Health Care System in Dallas.

Dr. Lederer works to train faculty in what she considers the nephrologists' tradition: mentorship, exceptional clinical skills, and superb research achievements. She is an active physician-scientist whose research centers on divalent metabolism. She oversees a basic science research laboratory to study regulation of kidney phosphate transport and a clinical research program in the modeling of CKD-MBD, funded by the Department of Veterans Affairs Merit Review Board.

Dr. Lederer believes the medical landscape, the role of medical schools, and the focus of research efforts are undergoing dramatic change and that organizations, such as ASN, must ensure that the kidney community is quickly apprised of changes that will affect our practice in all settings and receives informed analysis of the impact of these changes. A past president of ASN, she has served the organization in numerous roles, including on the ASN Council and as a member on the following committees: Communications, Program, Nominations, Abstract Selection, Training Program Directors Executive, Women in Nephrology Professional Development Seminar Organizing, and In-Training Examination Writing. She has served as editor-at-large for *CJASN* and is currently a section editor for *Clinical Nephrology, Current Opinion in Nephrology and Hypertension,* and *eMedicine: Nephrology.*

She has published many peer-reviewed articles and authored or co-authored chapters in numerous books, including *Essentials of Chronic Kidney Disease* and *Principles of Geriatric Medicine and Gerontology*.

Dr. Lederer has won numerous teaching, mentorship, and research awards and recently received the Excellence in Patient Care award from the National Kidney Foundation of Kentucky.

She is a graduate of Baylor College of Medicine, where she also completed her residency and nephrology fellowship. Dr. Lederer is a United Network for Organ Sharing-certified transplant physician.

Patient Advocate Will Speak on Education for Transplant Recipients

Patrick O. Gee, Sr., PhD

A transplant patient with a challenging story to tell will speak on "Incorporating Mental Health Practices by Increasing Psychosocial Education for Kidney Recipients" in the Celeste Castillo Lee Memorial Lectureship on Friday, November 4.

The presenter will be Patrick O. Gee, Sr., PhD, who is the founder and chief executive hope dealer at iAdvocate, a nonprofit, faith-based health and wellness organization. He is also an ordained minister at Mountain Movers Ministry in Richmond, VA. He retired from his position as chief of security at the Virginia Department of Corrections in 2008.

Dr. Gee's end stage kidney disease from diabetic kidney disease was treated with peritoneal hemodialysis until he received a transplant in 2017. Upon waking from the transplant surgery, he discovered that his newly transplanted kidney was not functioning due to a delayed graft function. As a result, he had to endure 24 hours of hemodialysis every other day until his kidney started to work. Five days after his surgery, his physician told him that he needed additional surgery to remove a blood clot in his neck. Three days after that procedure, he underwent surgery for a hemorrhaging problem, and 17 days later, he had a fourth surgery to create a laparoscopic peritoneum window so he could drain internally.

After four surgeries and 33 days in the hospital, his newly transplanted kidney was still not working. Dr. Gee's new kidney began to function minimally 47 days after surgery, but it took 2½ years before his newly transplanted kidney worked well enough for him to urinate normally.

Dr. Gee uses his personal experiences to teach, coach, mentor, and educate others on how best to manage their difficult situations. He is an advocate for those living with chronic kidney disease and the morbid conditions that contribute to this disease, such as diabetes, cardiovascular disease, hypertension, and obesity. He is particularly passionate about speaking on behalf of the underserved, undervalued, and disenfranchised communities of color to give them a voice in their quality of life and equitable health care access.

To this end, he serves in several capacities. He is a patient representative for the ASN Diabetic Kidney Disease Collaborative Task Force; a vice chair of the Patient and Family Partnership Council of the Kidney Health Initiative; on advisory boards of Home Dialyzors United, APOL1 Long-term Kidney Transplantation Outcomes Consortium, Center for Dialysis Innovation, and Patient & Family Centered Care Partners; and on US Food and Drug Administration and National Institute of Diabetes and Digestive and Kidney Diseases committees on diversity, inclusion, and outreach in medical device development; clinical research; and transplants.

Dr. Gee received a doctoral degree in justice, law, and criminology from American University.

STATE-OF-THE-ART LECTURE

Moderna Executive to Address Uses of mRNA

Melissa J. Moore, PhD

The chief scientific officer of Moderna will deliver a state-of-the-art lecture, titled "mRNA as Medicine," on Saturday, November 5.

The speaker, Melissa J. Moore, PhD, joined Moderna in 2016 as chief scientific officer of platform research after running academic research laboratories for 23 years. She played a key role in the development of Moderna's mRNA-based COVID-19 vaccine, the second COVID-19 vaccine to gain U.S. Food and Drug Administration approval. She directs research into mechanisms to deliver therapeutic mRNAs and into ways to increase their functional output and longevity.

Dr. Moore began working on RNA metabolism during her postdoctoral training at the Massachusetts Institute of Technology (MIT) in Cambridge. During her 23 years as a faculty member, first at Brandeis University and then at the University of Massachusetts Chan Medical School (UMMS), her research explored a broad array of topics related to the roles of RNA and RNA-protein complexes in gene expression related to many diseases, including cancer, neurodegeneration, and preeclampsia.

Her academic work was known for its mechanistic and structural analyses of spliceosomes and mRNA proteins, co-discovery of the exon junction complex, and studies of intracellular RNA transport and quality control pathways. She was also instrumental in developing multiple enabling technologies for the field, including methods for introducing site-specific modifications into long RNA molecules and single-molecule methods for observing the dynamics of ribonucleoprotein complex assembly and disassembly.

At UMMS, Dr. Moore was professor of biochemistry and molecular pharmacology, Eleanor Eustis Farrington chair in cancer research, and a long-time investigator at the Howard Hughes Medical Institute. She was also a founding co-director of UMMS's RNA Therapeutics Institute and was instrumental in creating the Massachusetts Therapeutic and Entrepreneurship Realization initiative, a program to facilitate the translation of UMMS discoveries into drugs, products, technologies, and companies.

Dr. Moore is currently on the board of directors of Tessera Therapeutics, as well as several scientific advisory boards. She co-founded two companies (Comanche Biopharma and Via Scientific) to further initiatives begun at UMMS. She has received many accolades, including the RNA Society Lifetime Achievement in Science Award.

Dr. Moore received her doctorate in biological chemistry, specializing in enzymology, from MIT.

Mark Perazella to Be Given Robert G. Narins Award for Contributions in Education

Mark A. Perazella, MD, FASN

Mark A. Perazella, MD, FASN, will receive the Robert G. Narins Award for his many efforts in the education and training of the next generation of nephrologists on Saturday, November 5.

Dr. Perazella is professor of medicine at Yale University School of Medicine and a nephrologist at the West Haven VA Medical Center in West Haven, CT.

His academic career has centered on his role as a clinician and educator. He completed a 12-year term as director of the Yale Nephrology Fellowship Training Program. He is currently director of the Acute Dialysis Program at Yale New Haven Hospital and medical director of the Yale Physician Associate Program and Yale Online Physician Assistant Program.

Dr. Perazella co-chaired the National Kidney Foundation Spring Clinical Meetings in 2019 and chaired its 2020 virtual Spring Clinical Meetings. He is former education co-director for the ASN Board Review Course. He served a 6-year term as a member of the American Board of Internal Medicine Nephrology Subspecialty Board and Exam Writing Committee. He also served on the ASN Continuing Professional Development and Post-Graduate Education Committees and chaired the ASN Onco-Nephrology Forum Group. He served on the ASN Training Program Directors Executive Committee and NKF Education Committee. He is a committee member for ASN Kidney Week for 2022 and will be a co-chair for ASN Kidney Week in 2023.

Dr. Perazella is active in editorial work. He is deputy editor of *Kidney360*, co-editor-in-chief of the *Journal of Onco-Nephrology*, and section editor for acute kidney injury for *Clinical Nephrology*. He also serves on the editorial boards of *CJASN*, *The American Journal of Medicine*, and *American Journal of Kidney Diseases*. He was an assistant editor for *Seminars in Dialysis* and associate editor of *CJASN*.

He has published more than 320 articles, written numerous book chapters, and co-edited five textbooks, including *Nephrology in 30 Days, Primer on Kidney Diseases, Current Diagnosis & Treatment: Nephrology & Hypertension, Onco-Nephrology,* and *Tubulointerstitial Nephritis*. His clinical areas of interest are drug-induced kidney disease, onco-nephrology, HIV-related kidney disease, and complications of hemodialysis.

Dr. Perazella obtained his medical degree at New York Medical College. He did his residency at the Yale Primary Care Residency Program and fellowship at Yale University/Yale New Haven Hospital.

ASN to Bestow Belding H. Scribner Award on Phyllis August

Phyllis August, MD, MPH

The Belding H. Scribner Award will be tendered on Saturday, November 5, to Phyllis August, MD, MPH, for her career-long contributions to the practice of nephrology. Dr. August is professor of medicine, public health, and obstetrics and gynecology; Ralph A. Baer, MD, Professor of Research in Medicine; and director of nephrology and hypertension at Weill Cornell Medical College. She is also director of the Nephrology Fellowship Program at New York Presbyterian/Weill Cornell and director of the Theresa and Eugene M. Lang Center for Research and Education at New York Presbyterian/Queens.

Established in 1995, the Belding H. Scribner Award is presented to individuals who have made outstanding contributions to the care of patients with renal disorders or have substantially influenced the clinical practice of nephrology. Dr. August is the first woman to garner this honor in recognition of her pioneering clinical and research contributions in kidney physiology during healthy pregnancy and in preeclampsia.

Dr. August's research focuses on the study of blood pressure and kidney function in normal and hypertensive pregnancy, the renal hemodynamic effects of antihypertensive drugs, the pathogenesis of preeclampsia, the role of transforming growth factor beta in hypertension, diabetic kidney disease, and clinical trials for the reduction of morbidity and mortality in patients with type 2 diabetes. As director of the Lang Center for Research and Education, she oversees sponsored clinical research across a broad range of subspecialties, including maternal-fetal medicine, cardiovascular disease, chronic kidney disease, diabetes, and cancer.

Dr. August is recognized as the leading nephrology expert on the physiology of kidney function during pregnancy. She was the first to report hypocalciuria in women with preeclampsia approximately 35 years ago. Her group also demonstrated the role of abnormal vitamin D levels. These findings led to changes in calcium supplementation for pregnant women throughout the world. She characterized the longitudinal changes in the renin, angiotensin, and aldosterone pathway in hypertensive pregnant women and demonstrated that women with superimposed preeclampsia have suppressed renin and aldosterone.

Dr. August led and participated in several committees to create guidelines for the management of hypertension during pregnancy, and her research directly impacted the guidelines. She has edited several authoritative textbooks on these topics and was the original author of six UpToDate chapters on hypertension in pregnancy, which she continues to edit.

Dr. August has served on numerous ASN committees and was associate editor of *JASN* for 5 years.

She has been honored with the Lester Hoenig Award of the National Kidney Foundation, the Outstanding Physician Award of the Preeclampsia Foundation, and the New York-Presbyterian Miriam G. Wallach Award for Excellence in Humanistic Medical Care.

Dr. August graduated from Yale Medical School. She completed her internship at Yale New Haven Hospital and residency and fellowship in internal medicine, nephrology, and hypertension at the New York Hospital-Cornell Medical Center. She received a Masters degree in public health from the Harvard T.H. Chan School of Public Health.

Pioneering Researcher Jeff Sands to Receive Smith Award

Jeff M. Sands, MD, FASN

Prominent investigator Jeff M. Sands, MD, FASN, will be presented the Homer W. Smith Award on Saturday, November 5. This award recognizes outstanding contributions to understanding how kidneys function in normal and diseased states.

Dr. Sands will speak on "Urea Transport to Nephrogenic Diabetes Insipidus: Using Physiology to Develop Novel Therapy." He is director of the Division of Renal Medicine and Juha P. Kokko Professor of Medicine at Emory University School of Medicine. He has also served Emory as executive vice-chair of medicine and associate dean for clinical and translational research.

Dr. Sands' research group has made major contributions to our understanding of the molecular physiology of urea transporters, aquaporins, and the urine-concentrating mechanism.

The researchers identified urea transporters and defined how they are regulated in ways that have revolutionized our understanding of how urine is concentrated. Dr. Sands' team showed that vasopressin, a key hormonal regulator of the urine-concentrating mechanism, not only affects water transport within minutes but also stimulates urea transport using perfused rat terminal inner medullary collecting ducts. His group also investigated whether there are non-vasopressin-mediated pathways that increase urea and water transport as a potential strategy to treat congenital nephrogenic diabetes insipidus—work that led to the discovery of an investigational drug that increases urine-concentrating ability and the formation of a startup company to advance the work on this drug.

Among many examples of his professional service, Dr. Sands chaired an ASN Annual Meeting Program Committee and the American Heart Association Kidney Council and was a member of the National Institute of Diabetes and Digestive and Kidney Diseases Board of Scientific Councilors and president of the American Physiological Society (APS). He also served as editor-in-chief of the *American Journal of Physiology-Renal Physiology*.

Dr. Sands has received several honors, including the Distinguished Alumnus Award from Boston University School of Medicine, the Carl W. Gottschalk Distinguished Lectureship from the APS Renal Section, the Distinguished Achievement Award from the American Heart Association, the Barry M. Brenner Endowed Lectureship from ASN, and an honorary degree from Aarhus University in Denmark.

Dr. Sands is a graduate of Boston University School of Medicine. He completed an internal medicine residency at the University of Chicago, followed by research fellowships at the National Heart, Lung, and Blood Institute. He then completed a clinical nephrology fellowship at Emory University, which he joined as an assistant professor in 1989. He was promoted to associate professor in 1993 and to professor in 1998.

Researcher to Describe Healthy Kidney Development

Andrew P. McMahon, PhD

A leading researcher in mechanisms of organ formation and function will deliver the Barry M. Brenner, MD, Endowed Lectureship on "Developmentally Programming to a Healthy Kidney" on Saturday, November 5.

The speaker will be Andrew (Andy) P. McMahon, PhD, who is the W.M. Keck Provost and a university professor with the Keck School of Medicine at the University of Southern California (USC). He also chairs the Department of Stem Cell Biology and Regenerative Medicine and directs the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research.

Dr. McMahon's research has provided fundamental insight into cell interactions that drive the assembly of multiple mammalian organ systems with a focus on the central nervous system, skeleton, and kidney. Discoveries by the McMahon laboratory have illuminated normal processes of organogenesis and tissue repair as well as the misregulation of developmental pathways in cancer. The McMahon group's early kidney studies identified some of the foundational signals in induction, patterning, and morphogenesis of the mammalian kidney. Recent studies have extended a developmental understanding from the mouse to the human kidney, promoted human disease modeling through stem cell-derived organoid systems, and identified molecular and cellular processes at play in kidney repair.

Dr. McMahon began his research career in 1984 as a staff scientist at the National Institute for Medical Research in London. In 1988, he joined the Roche Institute of Molecular Biology in Nutley, NJ, as an assistant member. He became a full member and department chair in 1992. The next year, Dr. McMahon became a professor of molecular and cellular biology in the Faculty of Arts and Sciences at Harvard University. During his 19-year career at Harvard, he was a professor of science, chair of the Department of Cell and Developmental Biology, founding member of the Department of Stem Cell and Regenerative Biology, and principal investigator of the Harvard Stem Cell Institute. In 2012, he moved from Harvard to his current position at USC.

Among his many professional service positions, he has served on the editorial board of several journals and is currently on the editorial board of *JASN*. Dr. McMahon is a member of the National Academy of Sciences and a fellow of the American Association for the Advancement of Science, American Academy of Arts and Sciences, European Molecular Biology Organization, and Royal Society.

He received his doctorate from University College London, followed by postdoctoral research at the California Institute of Technology.

STATE-OF-THE-ART LECTURE

MacArthur Fellow to Speak on Wearable and Implantable Medical Devices

John A. Rogers, PhD

A prolific inventor and entrepreneur will present a state-of-the-art lecture on "Wearable Microfluidic Devices and Implantable Electronic Systems for Kidney Health" on Sunday, November 6.

The speaker will be John A. Rogers, PhD, who is the Louis A. Simpson and Kimberly K. Querrey professor in the Departments of Materials Science & Engineering, Biomedical Engineering, Neurological Surgery, Electrical and Computer Engineering, Mechanical Engineering, and Chemistry at Northwestern University Feinberg School of Medicine in Chicago, IL, where he is also director of the Querrey Simpson Institute for Bioelectronics.

Dr. Rogers has published more than 850 papers and is co-inventor on more than 100 patents, some 70 of which are licensed and in active use by large companies or startups that he co-founded. His research includes fundamental and applied aspects of nano- and molecular-scale fabrication, as well as materials and patterning techniques for unusual electronic and photonic devices, with an emphasis on bio-integrated and bio-inspired systems.

His research seeks to understand and exploit "soft" materials, such as polymers, liquid crystals, and biological tissues, as well as hybrid combinations of them with unusual classes of micro/nanomaterials in the form of ribbons, wires, membranes, and tubes.

His team has developed wearable electronics that bend and stretch with the human body. These devices include a flexible implant that supplies electrical stimulation to premature infants' nerves and dissolves after it is no longer needed, as well as a skin-like sticker that monitors babies' vital signs in Neonatal Intensive Care Units. In partnership with the Bill & Melinda Gates Foundation, Dr. Rogers' team has deployed thousands of these new devices across countries in Africa and Asia to monitor the health of newborns and their mothers.

His research has been recognized by many awards, including a MacArthur Fellowship, the Lemelson-MIT Prize, the Smithsonian American Ingenuity Award in the Physical Sciences, the Benjamin Franklin Medal from The Franklin Institute, and a Guggenheim Fellowship.

Dr. Rogers received Masters degrees in physics and chemistry and a doctorate in physical chemistry from the Massachusetts Institute of Technology (MIT). From 1995 to 1997, he was a junior fellow in the Harvard University Society of Fellows.

He joined Bell Laboratories as a member of the technical staff in the Condensed Matter Physics Research Department in 1997 and served as director of this department from 2000 to 2002. He then spent 13 years on the faculty of the University of Illinois at Urbana-Champaign, including as director of the Frederick Seitz Materials Research Laboratory. He joined Northwestern in 2016.

Blagg Lecture to Focus on Dialysis for Undocumented Immigrants

Lilia Cervantes, MD

Public health expert and advocate Lilia Cervantes, MD, will deliver the Christopher R. Blagg, MD, Endowed Lectureship in Kidney Disease and Public Policy on Sunday, November 6. The topic will be "Dialysis for Patients in the Undocumented Immigrant Community in the United States."

Dr. Cervantes is the director of immigrant health and associate professor of medicine at the University of Colorado Anschutz Medical Campus in Denver.

She spearheaded an innovative change to a Medicaid payment rule in Colorado to give undocumented patients with kidney failure access to life-saving maintenance dialysis. One event that crystallized the need for this change was the death of a patient who was ineligible for Medicaid because of her undocumented status and therefore unable to receive regular dialysis treatments. Such patients could receive dialysis only in the emergency room when their health was in critical condition. This policy led Dr. Cervantes to pivot her career from clinical work to research and advocacy for the expansion of access to standard dialysis for undocumented and uninsured immigrants.

Dr. Cervantes conducted research to document the enormous human and economic costs of the exclusionary policy, developed a coalition of allies, and proposed a policy remedy. Thanks to the work of Dr. Cervantes and her team, the state of Colorado in February 2019 announced a policy change that expanded access to standard three-times-per-week dialysis care for patients with kidney failure who previously had to rely on emergency-only treatment.

Her background as a first-generation Latina shaped her commitment to becoming a physician as well as her focus on community service, health policy activism, and health equity research.

"I grew up in a neighborhood that is very poor, where the life expectancy is about 12 years shorter [than it is in] a neighborhood that's just five miles away," Dr. Cervantes said. "From a very young age, I knew that I wanted to be a physician. I wanted to improve the well-being of my community."

Her efforts have garnered national attention and partnerships, leading to efforts to enable routine dialysis for underserved patients in several other states. Following this defining experience, Dr. Cervantes' research and advocacy have focused on eliminating structural racism to reduce kidney health disparities.

She has received more than 15 awards for her service to her community and is a member of nine civic and community activity boards.

Dr. Cervantes completed her medical degree and internal medicine residency at the University of Colorado School of Medicine. She has worked as a hospitalist at Denver Health, the safety-net hospital for the city of Denver, for more than 12 years.

ASN Announces Midcareer Award Winners

ASN's Midcareer Awards recognize individuals who have made substantial and significant contributions in a variety of areas early in their professional lives.

These awards recognize up to three winners in each of five categories: clinical service, education, leadership, mentorship, and research.

Distinguished Clinical Service Award

Jocelyn S. Garland, MD

Dr. Garland is associate professor of medicine and nephrology as well as associate professor of obstetrics and gynecology at Queen's University in Kingston, Ontario, Canada, where she has worked since she began her career in academic medicine in 2003. She is also medical director for glomerulonephritis/pregnancy in the Renal Disease Clinic and medical director of plasmapheresis at Kingston Health Sciences Centre.

Dr. Garland's nephrology practice specializes in rare kidney diseases. She has held many administrative roles and contributed to scholarly work with 60 invited lectures and 77 peer-reviewed articles and abstracts, many involving her supervision of medical learners. She is recognized as a national clinical expert in the field of thrombotic microangiopathy, and she often consults with colleagues to help others manage this rare disease.

As medical director of the Glomerulonephritis Clinic, she aims to improve access and quality of care for patients who have kidney impairment secondary to glomerulonephritis-related diseases. Dr. Garland also actively participates in collaborative research initiatives, including clinical practice guidelines and clinical trials.

Her excellent patient care has been recognized with many awards, including the Ontario Renal Network/Cancer Care Ontario Provincial Human Touch Award, the Royal College Physicians and Surgeons of Canada Specialist of the Year Award for her work in thrombotic microangiopathy, and the Kingston Health Sciences Medical Staff Association's Outstanding Clinician of the Year. She has also received several teaching awards from both undergraduate and postgraduate medical learners.

She received her medical degree from Memorial University of Newfoundland and Masters degrees in epidemiology and biostatistics from both Queen's University and the University of Western Ontario.

Distinguished Educator Award

Steven C. Cheng, MD

Dr. Cheng is professor of medicine in the Division of Nephrology at Washington University in St. Louis, MO, where he has been the training program director since 2011.

He served on the ASN Training Program Directors Executive Committee and is currently on the ASN Workforce and Training Committee. He has also led special sessions during program director retreats and town halls on educational innovations, career paths, procedural requirements, and the nephrology match. As the current chair of the ASN Match Oversight Task Force, Dr. Cheng plays a key role in overseeing the recruitment of fellows to U.S. training programs.

Dr. Cheng is also deeply involved in undergraduate medical education as a course director and chair of the Phase 1 Operations Committee of the Washington University School of Medicine gateway curriculum. In this role, he has helped to design a curriculum that integrates basic science and clinical practice while also equipping students to navigate health systems and address disparities in patient care. His renal module is popular among students for its clear presentation of material and opportunities to consider the effects of chronic kidney disease by meeting with patients, debating end stage kidney disease options, and discussing the intersection of race and kidney diseases.

Dr. Cheng has received numerous awards, including the Samuel R. Goldstein Leadership Award in Medical Student Education and the Sydney S. Pearl Award for Inspirational Teaching.

He received his medical degree and completed his internal medicine residency and internship at Northwestern University, followed by a nephrology fellowship at Washington University.

Matthew A. Sparks, MD, FASN

Dr. Sparks is associate professor of medicine at Duke University in Durham, NC, and director of its Nephrology Fellowship Program.

He is a founder of the Society for Early Education Scholars (SEEDS) program, which is a yearlong curriculum across all disciplines in the Duke Department of Medicine for fellows who plan careers as clinician-educators or education scholars. He is co-director of the scientific communications course offered by the Duke Clinical Research Training Program.

Dr. Sparks is a founding faculty member and program director of the Nephrology Social Media Collective Internship and member of the Board of Directors of the Nephrology Journal Club—NephJC—a nonprofit organization dedicated to enhancing free online medical education in nephrology. He is a faculty lead of the Renal Fellow Network and is a member of The Nephron Segment Podcast.

Dr. Sparks is co-creator of NephMadness, an educational initiative modeled after the U.S. college basketball tournament but using nephrology concepts. He is an advisory board member of NephSIM—a free, mobile-optimized nephrology teaching tool that includes case-based learning, infographics, and tutorials—and co-director of the virtual mentoring program, NephSIM Nephrons.

He has been a member of several national committees for both ASN and the American Heart Association. He also serves as education director for KIDNEYcon, an annual hands-on conference dedicated to advances in nephrology. He is a member of the American Board of Internal Medicine Nephrology Board and is on the editorial boards of several publications, including *CJASN*, *American Journal of Kidney Diseases*, *Kidney Medicine*, *Kidney360*, and *ASN Kidney News*.

Dr. Sparks received his MD and completed his residency in internal medicine at the University of Arkansas for Medical Sciences. He did his nephrology fellowship at Duke University Medical Center.

Distinguished Leader Award

Kirk N. Campbell, MD, FASN

Dr. Campbell is the Irene and Dr. Arthur M. Fishberg Professor of Medicine at the Icahn School of Medicine at Mount Sinai in New York City, where he is also director of the Nephrology Fellowship Program and vice chair for diversity, equity, and inclusion in the Department of Medicine. He co-chairs the ASN Kidney Week 2022 Education Committee.

Dr. Campbell leads a National Institutes of Health (NIH)-funded research program focused on podocyte cell biology, experimental glomerular disease, and clinical trials in rare kidney diseases. The work centers on understanding the underlying mechanisms of glomerular disease progression and identifying targets for therapeutic intervention. He has been a principal investigator for clinical trials, testing novel agents for focal segmental glomerulosclerosis, IgA nephropathy, lupus nephritis, and membranous nephropathy.

He is a member of the editorial boards of *Kidney360*, *Kidney International, American Journal of Kidney Diseases*, *Frontiers in Medicine*, and *American Journal of Physiology–Renal Physiology*.

As director of the Nephrology Fellowship Program, he helped expand research training opportunities and established new subspecialty training tracks in critical care nephrology, geriatric nephrology, and home dialysis.

A former president of The New York Society of Nephrology, Dr. Campbell is a member of the Board of Directors of the NephCure Foundation, the Medical Advisory Board of the National Kidney Foundation Serving Greater New York, and the NIH Pathobiology of Kidney Disease study section. He has served ASN on the Diversity, Equity, and Inclusion Committee; Grants Review Committee; and Continuous Professional Development Committee. He is a member of the American Kidney Fund's Health Equity Coalition Subgroup focused on advancing strategies for inclusive clinical trial enrollment.

Dr. Campbell received his medical degree from the University of Connecticut, did his residency at Yale University, and completed his nephrology fellowship at the Icahn School of Medicine at Mount Sinai.

Sunday, November 6, 2022

PLENARY SESSION

Elke Schaeffner, MD, MSc

Dr. Schaeffner is professor of nephrology and health care research, as well as an epidemiologist at the Institute of Public Health, Charité–Universitätsmedizin Berlin, Germany.

She is also deputy director of the Berlin School of Public Health, where she played a pivotal role in establishing a new Master of Science Program in Public Health and a Doctoral Program in Health Data Sciences.

Her primary fields of research are renal epidemiology and aging, with a particular focus on chronic kidney disease (CKD) in an aging society and biomarkers for assessing kidney function. She is principal investigator of the landmark Berlin Initiative Study, a population-based cohort study investigating the epidemiology of CKD in more than 2000 elderly patients over several years. With its serial glomerular filtration rate (GFR) and other measurements, the study has provided unparalleled high-quality primary data about the natural course of kidney function in elderly persons.

Dr. Schaeffner is a co-founder of the European Kidney Function Consortium, a group focused on optimizing the diagnosis of CKD using novel non-creatinine-based biomarkers and standardized measurements of GFR.

Dr. Schaeffner established a popular 2-day workshop in epidemiological methods for clinicians that has been an integral part of the annual meeting of the German Society of Nephrology for the past decade.

She serves as international editor on the editorial board of the *American Journal of Kidney Diseases*, on the Kidney Disease: Improving Global Outcomes (KDIGO) Workgroup updating the guidelines for evaluation and management of CKD, and on the European Renal Best Practice Guidelines group.

Dr. Schaeffner studied medicine at the University of Freiburg in Germany and obtained her Master of Science in epidemiology at the Harvard T.H. Chan School of Public Health in Boston, MA.

Suzanne Watnick, MD, FASN

Dr. Watnick is the chief medical officer at Northwest Kidney Centers and a professor of medicine in the Division of Nephrology at the University of Washington. She also practices in the Veterans Affairs Puget Sound Health Care System in Seattle, WA.

She has filled important leadership roles with ASN. She spearheaded the inaugural virtual Dialysis Core Curriculum and was instrumental in the development of the first Dialysis Practice Improvement Module. She has served on many ASN committees, including the Public Policy Board, a Home Dialysis Task Force, the Policy and Advocacy Committee, the Training Program Directors Executive Committee, and the Postgraduate Education Committee. She currently serves on the ASN Quality Committee and represents ASN at Kidney Care Partners.

Dr. Watnick regularly represents ASN and the kidney community in meetings with legislators and regulators to advocate for patient-centered care. She has worked tirelessly to bring together groups, such as ASN and the National Kidney Foundation, to work for better kidney care policy.

She served on the Kidney Disease: Improving Global Outcomes (KDIGO) Executive Committee and the American Board of Internal Medicine Nephrology Board and is on the editorial board of *CJASN*.

Dr. Watnick has also been a leader in responding to the COVID-19 pandemic. After a Northwest Kidney Centers dialysis patient was the first reported U.S. death from COVID-19, Dr. Watnick implemented rigorous plans to safely treat dialysis patients. She shared what she learned with the Centers for Disease Control and Prevention and with the kidney community nationally.

Dr. Watnick received her medical degree from the University of Massachusetts Chan Medical School in Worcester, followed by an internship and residency in internal medicine and a clinical fellowship in nephrology at the University of California, San Francisco. She then completed clinical and research fellowships in nephrology at Yale University. Before moving to Seattle, she spent 16 years at Oregon Health & Science University and the Portland VA Medical Center, where she served several roles, including as the training program director of the fellowship program.

Distinguished Mentor Award

Michelle M. Estrella, MD, MS

Dr. Estrella is professor of medicine at the University of California, San Francisco (UCSF); renal section chief at the San Francisco Veterans Affairs Health Care System; and executive director of the Kidney Health Research Collaborative.

Her research program aims to improve the understanding of kidney diseases and to develop strategies that alleviate the burden of kidney diseases. This work focuses on the identification and clinical translation of kidney health biomarkers that could lead to earlier detection and management of kidney diseases, as well as the development of strategies to optimize health care delivery and clinical outcomes in kidney diseases.

In addition to patient care and clinical research, Dr. Estrella's career centers on mentorship and sponsorship of young investigators, particularly those from groups that are underrepresented in medicine. She has mentored several undergraduate and medical students, more than 20 fellows, and seven early-stage faculty members.

Dr. Estrella is also dedicated to addressing inequities in academia. When she was at Johns Hopkins, she served on task forces that fostered gender equity and diversity in the School of Medicine community. At both Hopkins and UCSF, she has worked to recruit trainees from diverse racial, ethnic, and economic backgrounds through her leadership roles in the Residency, Fellowship, and Training Program Selection Committees.

Dr. Estrella obtained her medical degree at The University of Texas Health Science Center at Houston. She completed her clinical training in internal medicine and nephrology at The Johns Hopkins Hospital in Baltimore, MD. She also obtained a Masters degree in health science at the Johns Hopkins Bloomberg School of Public Health.

Karen M. Warburton, MD, FASN

Dr. Warburton is associate professor of medicine and a nephrologist specializing in kidney and pancreas transplantation at the University of Virginia (UVA) Health System in Charlottesville. In addition to her clinical role, Dr. Warburton is the director of the Clinician Wellness Program, director of Graduate Medical Education Advancement, and vice chief of faculty development in the Division of Nephrology.

Before joining UVA in 2016, she spent 17 years at the University of Pennsylvania, where she served as associate program director for the Internal Medicine Residency and Nephrology Fellowship Training Programs for several years. In those roles, she developed expertise in coaching and remediation of struggling learners. She developed and chaired successful remediation programs at both institutions.

In her role as a director of the Clinician Wellness Program, Dr. Warburton works with faculty and trainees to promote personal and professional well-being, to find meaning in their work as a means of reducing burnout and promoting and maintaining engagement, and to foster effective interpersonal communication by increasing self-awareness and promoting emotional intelligence skills. She provides clinical assessment and counseling for stress, substance use, anxiety, and depression among physicians.

She served for 5 years as the organizing chair for ASN's Kidney Students and Residents (STARS) Program, which is designed to foster interest in nephrology careers through a mentored experience at ASN Kidney Week. She also directed a full-day workshop at a nephrology training directors retreat on coaching and remediation for struggling trainees.

Dr. Warburton received her medical degree from the University of North Carolina School of Medicine, followed by an internship, residency, chief residency, fellowship in nephrology, and fellowship in kidney and pancreas transplantation at the University of Pennsylvania.

Distinguished Researcher Award

Peter P. Reese, MD, PhD

Dr. Reese is professor of medicine at the University of Pennsylvania Perelman School of Medicine, Philadelphia, with secondary appointments in epidemiology and medical ethics. His clinical practice focuses on the care of kidney transplant recipients and living kidney donors.

Dr. Reese's research focuses primarily on developing effective strategies to increase access to kidney transplantation, improving the process of selecting and caring for living kidney donors, determining outcomes of health policies on vulnerable populations with kidney diseases (including the elderly), testing strategies to improve important health behaviors such as medication adherence, and exploring transplant ethics.

His contributions include co-leading the first kidney and heart trials of transplanting organs from donors with hepatitis C virus infection into uninfected recipients, followed by treatment with antiviral agents. This practice became widely adopted by North American transplant centers and enabled thousands of patients to receive transplants using organs that had been discarded in the past. Dr. Reese has also contributed many studies about ways to expand kidney transplantation through the wider use of kidneys from older and comorbid donors.

His policy contributions include serving as chair of the Ethics Committee and member of several other committees at the United Network for Organ Sharing.

Dr. Reese received his MD from Johns Hopkins School of Medicine, followed by an internal medicine internship, residency, chief residency, and renal fellowship at Brigham and Women's Hospital in Boston, MA. He completed fellowships in nephrology and transplant nephrology at the University of Pennsylvania Perelman School of Medicine. He also obtained a Masters degree in epidemiology from the University of Pennsylvania and a doctorate in epidemiology from the University of Paris.

Alexander Staruschenko, PhD, FASN

Dr. Staruschenko is professor and director of the Hypertension and Kidney Research Center at the University of South Florida, Tampa.

The research in his laboratory focuses on understanding the mechanisms controlling ion channel activity and electrolyte homeostasis in blood pressure control and kidney diseases. His laboratory is supported by the National Institutes of Health and other prestigious funders, and his research has been recognized nationally. He has published more than 150 peer-reviewed manuscripts in leading nephrology and hypertension journals and presented his research at more than 100 local, national, and international seminars and meetings.

Dr. Staruschenko has mentored a number of students, postdoctoral fellows, and junior faculty, several of whom have established their own independent laboratories.

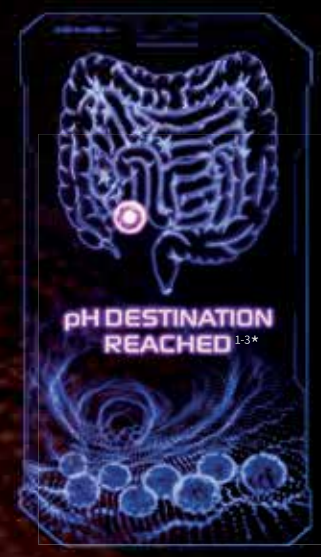
He is a dedicated contributor to the activities of several national societies. He is a deputy editor of the *American Journal of Physiology–Renal Physiology* and a member of the editorial boards of several journals. He chairs the American Heart Association Council on the Kidney in Cardiovascular Disease.

His research has been recognized with the Carl W. Gottschalk Research Scholar Award from ASN, a Young Scholar Award from the American Society of Hypertension, an Established Investigator Award from the American Heart Association, and Young Investigator Awards from the American Physiological Society.

Dr. Staruschenko received his PhD from the Institute of Cytology at the Russian Academy of Sciences in St. Petersburg. He completed a postdoctoral fellowship in renal physiology at The University of Texas Health Science Center at San Antonio.

For adults at risk of rapid disease progression,

TARPEYO: First and only treatment FDA approved to reduce proteinuria in IgA Nephropathy[1]



TARPEYO® (budesonide) delayed release capsules is designed to deliver treatment to an area of the ileum to target mucosal B cells, which are responsible for the production of galactose-deficient IgA1 antibodies, causing immunoglobulin A Nephropathy (IgAN).[1,2,4]

*Drug release is initiated in the ileum by the pH-dependent disintegration of the enteric coat.[1,3]

Indication

TARPEYO® (budesonide) delayed release capsules is a corticosteroid indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.

This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

Important Safety Information

Contraindications: TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis, have occurred with other budesonide formulations.

Warnings and Precautions

Hypercorticism and adrenal axis suppression: When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy *[see Dosing and Administration]* or switching between corticosteroids, monitor for signs of adrenal axis suppression.

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

Risks of immunosuppression: Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressive doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection; untreated fungal, bacterial, systemic viral, or parasitic infections; or ocular herpes simplex. Avoid exposure to active, easily transmitted infections (eg, chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.

TARPEYO®
(budesonide) delayed release capsules • 4 mg
DIRECT BY DESIGN

Designed to deploy in the ileum[1,2,4†]

- Designed to deliver treatment to the area of the ileum, including the Peyer's patches, where mucosal B cells are located
- Mucosal B cells express glucocorticoid receptors and produce galactose-deficient IgA1 antibodies, causing IgAN
- Through anti-inflammatory and immunosuppressive effects at the glucocorticoid receptor, TARPEYO can modulate B cell numbers and activity

Statistically significant reduction in UPCR with TARPEYO plus RASi vs RASi alone at 9 months[1‡§]

- **Primary endpoint:** Significant reduction (34%) in UPCR from baseline was achieved in the TARPEYO plus renin-angiotensin system inhibitor (RASi)-treated group (n=97) vs 5% with RASi alone (n=102) at 9 months[1‡§‖]
  - At the 12-month observational follow-up, a 53% reduction in UPCR from baseline was reported with TARPEYO plus RASi vs 9% with RASi alone[3§¶#]

Additional data presented beyond the primary endpoint of 9 months should be interpreted cautiously.

eGFR data with TARPEYO plus RASi vs RASi alone at 9 months

- **Secondary endpoint:** At 9 months, absolute change in eGFR was -0.6 mL/min/1.73 m^2 with TARPEYO plus RASi (n=97) vs -4.0 mL/min/1.73 m^2 with RASi alone (n=102)[3§**]

These interim secondary endpoint data were not prospectively controlled for multiplicity and need cautious interpretation. The clinical significance of these results is unknown. Confirmatory clinical trial results are required to draw any conclusions. It has not been established whether TARPEYO has demonstrated a benefit in slowing kidney function decline in patients with IgAN.[3]

Demonstrated safety profile

- 87% of patients in the TARPEYO plus RASi-treated group reported adverse reactions vs 73% of patients on RASi alone[1,3]
- In clinical studies, the most common adverse reactions of TARPEYO plus RASi (occurring in ≥10% of patients treated with TARPEYO plus RASi and at a higher incidence than RASi alone) were: hypertension, peripheral edema, muscle spasms, and acne[1,3]
- The safety profile is generally consistent with the well-established safety profile of the active ingredient, budesonide[3]

Study Design: NefIgArd is an ongoing, phase 3, randomized, double-blind, multicenter study to evaluate the efficacy and safety of TARPEYO 16 mg/day vs placebo in patients with primary IgAN as an addition to optimized RAS blockade therapy. Part A of the study (n=199) included a 9-month blinded treatment period and a 3-month follow-up period. The primary endpoint was UPCR at 9 months; eGFR was a secondary endpoint. Part B, a confirmatory validation study in which no treatment will be administered, will assess eGFR over 2 years.[1,3]

†It has not been established to what extent the efficacy of TARPEYO is mediated via local effects in the ileum vs systemic effects.[1]
‡31% reduction (95% CI, 16-42) in UPCR with TARPEYO plus RASi vs RASi alone (*P*=0.0001).[1††]
§All patients with a UPCR/eGFR reading regardless of use of prohibited medication at 9 months and 12 months.[1,3]
‖Adjusted geometric least squares mean ratio of UPCR relative to baseline were based on a longitudinal repeated measures model.[1]
¶49% reduction (95% CI, 37-58) in UPCR with TARPEYO plus RASi vs RASi alone.[3]
#Full analysis set (TARPEYO=97, placebo=102). Not all patients in the full analysis set contributed data at each postbaseline time point, including at 12 months.[3]
**Absolute changes derived from geometric least square mean ratios using the pooled baseline geometric mean.[3]
††The estimate of the ratio of geometric mean ratio of UPCR relative to baseline comparing TARPEYO 16 mg plus RASi with RASi alone was reported as percentage reduction along with the respective 95% confidence interval from the longitudinal repeated measures model and *P* values.[1]

Learn more about how TARPEYO works at TARPEYOhcp.com

Warnings and Precautions (cont'd)

Other corticosteroid effects: TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataracts, a family history of diabetes or glaucoma, or with any other condition in which corticosteroids may have unwanted effects.

Adverse reactions: In clinical studies, the most common adverse reactions with TARPEYO (occurring in ≥5% of TARPEYO patients and ≥2% higher than placebo) were hypertension (16%), peripheral edema (14%), muscle spasms (13%), acne (11%), dermatitis (7%), weight increase (7%), dyspnea (6%), face edema (6%), dyspepsia (5%), fatigue (5%), and hirsutism (5%).

Drug interactions: Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

Use in specific populations

Pregnancy: The available data from published case series, epidemiological studies, and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgAN. Infants exposed to in utero corticosteroids, including budesonide, are at risk for hypoadrenalism.

Please see brief summary of Full Prescribing Information on the adjacent pages.

References: 1. TARPEYO. Prescribing Information. Calliditas Therapeutics AB; 2021. **2.** Barratt J, Rovin BH, Cattran D, et al. Why target the gut to treat IgA nephropathy? *Kidney Int Rep.* 2020;5(10):1620-1624. doi:10.1016/j.ekir.2020.08.009 **3.** Data on file. Calliditas Therapeutics AB. **4.** Fellström BC, Barratt J, Cook H, et al. Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial. *Lancet*. 2017;389(10084):2117-2127. doi:10.1016/S0140-6736(17)30550-0

calliditas THERAPEUTICS

TARPEYO® (budesonide) delayed release capsules Brief Summary of Prescribing Information

4 CONTRAINDICATIONS

TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis have occurred with other budesonide formulations.

5 WARNINGS AND PRECAUTIONS

5.1 Hypercorticism and Adrenal Axis Suppression

When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy *[see Dosing and Administration (2)]* or switching between corticosteroids, monitor for signs of adrenal axis suppression.
Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure of oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B) *[see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)]*.

5.2 Risks of Immunosuppression

Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressant doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection, untreated fungal, bacterial, systemic viral or parasitic infections, or ocular herpes simplex. Avoid exposure to active, easily-transmitted infections (e.g., chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.
How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, consider therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG). If exposed to measles, consider prophylaxis with pooled intramuscular immunoglobulin (IG). If chickenpox develops, consider treatment with antiviral agents.

5.3 Other Corticosteroid Effects

TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma or cataracts, or with a family history of diabetes or glaucoma, or with any other condition where corticosteroids may have unwanted effects.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypercorticism and adrenal suppression *[see Warnings and Precautions (5.1)]*
- Risks of immunosuppression *[see Warnings and Precautions (5.2)]*
- Other corticosteroid effects *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety of TARPEYO has been evaluated in a randomized controlled study in 197 patients.
The most common adverse reactions reported in greater than or equal to 5% of TARPEYO-treated patients are listed in Table 1. The majority of adverse reactions were mild or moderate in severity.

Table 1: Reported adverse reactions occurring in greater than or equal to 5% of TARPEYO treated patients, and greater than or equal to 2% higher than Placebo

Adverse Reaction	TARPEYO 16 mg (N=97)	Placebo (N=100)
	n (%)	n (%)
Patients with any Adverse Reaction	84 (87)	73 (73)
Hypertension	15 (16)	2 (2)
Peripheral edema	14 (14)	4 (4)
Muscle spasms	13 (13)	4 (4)
Acne	11 (11)	2 (2)
Dermatitis	7 (7)	1 (1)
Weight increased	7 (7)	3 (3)
Dyspnea	6 (6)	0 (0)
Face edema	6 (6)	1 (1)
Dyspepsia	5 (5)	2 (2)
Fatigue	5 (5)	2 (2)
Hirsutism	5 (5)	0 (0)

Most adverse reactions that occurred at a greater incidence for TARPEYO compared to placebo were consistent with hypercortisolism.

7 DRUG INTERACTIONS

7.1 Interaction with CYP3A4 Inhibitors

Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors; e.g. ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine.
Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary The available data from published case series, epidemiological studies and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgA Nephropathy. Infants exposed to in-utero corticosteroids, including budesonide, are at risk for hypoadrenalism *(see Clinical Considerations)*.
In animal reproduction studies with pregnant rats and rabbits, administration of subcutaneous budesonide during organogenesis at doses approximately 0.3 times or 0.03 times, respectively, the maximum recommended human dose (MRHD), resulted in increased fetal loss, decreased pup weights, and skeletal abnormalities. Maternal toxicity was observed in both rats and rabbits at these dose levels *(see Data)*.
The estimated background risk of major birth defects and miscarriage of the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations *Disease-Associated Maternal and/or Embryo/Fetal Risk* IgA nephropathy in pregnancy is associated with adverse maternal outcomes, including increased rates of cesarean section, pregnancy-induced hypertension, pre-eclampsia and preterm delivery, and adverse fetal/neonatal outcomes, including stillbirth and low birth weight.
Fetal/Neonatal Adverse Reactions Hypoadrenalism may occur in infants born to mothers receiving corticosteroids during pregnancy. Infants should be carefully observed for signs of hypoadrenalism, such as poor feeding, irritability, weakness, and vomiting, and managed accordingly *[see Warnings and Precautions (5.1)]*.
Data *Animal Data* Budesonide was teratogenic and embryo-lethal in rabbits and rats.
In an embryo-fetal development study in pregnant rats dosed subcutaneously with budesonide during the period of organogenesis on gestation days 6 to 15 there were effects on fetal development and survival at subcutaneous doses up to approximately 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose (MRHD) on a body surface area basis).
In an embryo-fetal development study in pregnant rabbits dosed during the period of organogenesis on gestation days 6 to 18, there was an increase in maternal abortion, and effects on fetal development and reduction in litter weights at subcutaneous doses from approximately 25 mcg/kg (approximately 0.03 times the MRHD on a body surface area basis).
Maternal toxicity, including reduction in body weight gain, was observed at subcutaneous doses of 5 mcg/kg in rabbits (approximately 0.006 times the maximum recommended human dose on a body surface area basis) and 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose on a body surface area basis).
In a peri- and post-natal development study, subcutaneous treatment of pregnant rats with budesonide during the period from Day 15 post coitum to Day 21 post partum, budesonide had no effects on delivery, but did have an effect on growth and development of offspring. In addition, offspring survival was reduced and surviving offspring had decreased mean body weights at birth and during lactation at exposures ≥ 0.012 times the MRHD (on a mg/m^2 basis at maternal subcutaneous doses of 20 mcg/kg/day and higher). These findings occurred in the presence of maternal toxicity.

8.2 Lactation

Risk Summary Breastfeeding is not expected to result in significant exposure of the infant to TARPEYO. Lactation studies have not been conducted with oral budesonide, including TARPEYO, and no information is available on the effects of the drug on the breastfed infant or the effects on the drug on milk production. One published study reports that budesonide is present in human milk following maternal inhalation of budesonide *(see Data)*. Routine monitoring of linear growth in infants is recommended with chronic use of budesonide in the nursing mother. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TARPEYO and any potential adverse effects on the breastfed infant from TARPEYO, or from the underlying maternal condition.
Data One published study reports that budesonide is present in human milk following maternal inhalation of budesonide, which resulted in infant doses approximately 0.3% to 1% of the maternal weight-adjusted dosage and a milk to plasma ratio was approximately 0.5. Budesonide was not detected in plasma, and no adverse events were noted in the breastfed infants following maternal use of inhaled budesonide.
Assuming a daily average milk intake of about 150 mL/kg/day and a milk to plasma ratio of 0.5, the estimated oral dose of budesonide for a 5-kg infant is expected to be less than 2 mcg/day for a maternal dose of 16 mg TARPEYO. Assuming 100% bio-availability in the infant this is about 0.1% of the maternal dose and about 3% of the highest inhaled dose used clinically for asthma in infants.

8.4 Pediatric Use

The safety and efficacy of TARPEYO in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of TARPEYO did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Hepatic Impairment

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to budesonide *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*. Avoid use in patients with severe hepatic impairments (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

10 OVERDOSAGE

Reports of acute toxicity and/or death following overdosage of corticoids are rare.
In the event of acute overdosage, no specific antidote is available. Treatment consists of supportive and symptomatic therapy.

Please see Full Prescribing Information for TARPEYO at TARPEYOhcp.com

US-NEF-2100056-B v 2.0

Excellence in Patient Care: Promoting the Patient Voice in Pursuit of Evidence-Based Care

By Bonnie Freshly and Susan Stark

Excellence in Patient Care (EPC), organized in 2021, focuses on ASN's clinical priorities to provide high-quality care for people with kidney diseases. EPC relies on the insight of six exceptional patient advocates who inform its 11 projects, which aim to advance the use of best practices and evidence-based care for people with kidney diseases across the spectrum of care options. EPC includes the following wide-ranging projects: Nephrologists Transforming Dialysis Safety (NTDS), Diabetic Kidney Disease Collaborative (DKD-C); COVID-19 response; acute kidney injury (AKINow); Adult Immunization Project (AIP); Transforming Dialysis Access Together (TDAT); Home Dialysis Project (HDP); and Emergency Partnership Initiative (EPI).


Patrick O. Gee, Sr., PhD, JLC


Maria Levy


Quinetta Taylor, BCPA


Glenda Roberts

The shared foundation of these initiatives is science, a focus that has served EPC well, particularly through the beginning and height of the COVID-19 pandemic when the COVID-19 Response Team was created and promoted the call to "follow the science." This foundation of sound clinical decision-making has resulted in numerous publications, webinars, focus group sessions, online learning modules, and resources that have enriched the kidney community.

As EPC has continued to evolve, it has become evident that science is not enough—each clinical project comes to its best conclusion when the project considers the deep and multifactored impact of kidney diseases on patients. Acknowledging the central role of the patient voice led to significant roles for patient advocates on EPC project teams and the creation of educational products aimed at both patients and providers.

COVID may turn out to be a real benefit to our community, because it has given doctors a way to say that science is messy. COVID has shown that things change rapidly; we learn new things, so we do new things.

—Glenda Roberts

In a recent panel discussion, four patient advocates were asked about their involvement with EPC and the impact of integrating patient input with EPC project goals. Participants included Glenda Roberts; Quin Taylor, BCPA; Patrick O. Gee, Sr., PhD, JLC; and Marla Levy. All four patient advocates vigorously support the efforts of EPC to engage patients, applaud committee volunteers for their willingness to listen, and broadly recommend a heightened level of involvement for, and outreach to, patient advocates as EPC plans its next steps.

EPC COVID-19 resources calmed the kidney community in the midst of a pandemic…and showed that there was a community that actually cared. When you start seeing friends and peers and colleagues succumb because of an invisible virus…then when you see the urgency of folks scrambling, trying to understand…trying to provide as much information…it allowed patients to see the humane side of physicians that you wouldn't normally see in normal circumstances. It allowed patients to hear from physicians who said, 'I don't know, but we can find this out together.' I think it was very transparent. I think it was very safe, but it also promoted engagement. It built on the physician-patient dynamic that you need both components to get this done. [By] opening that [dynamic], look at the [number] of patients that now have found their voice because of these projects ... It's been a blessing to see that patients are gravitating to these tools … I applaud the efforts of EPC and think it really saved an entire community and brought some peace and stability to what could have been an erratic and out-of-control situation.

—Patrick O. Gee, PhD, JLC

These patient advocates describe EPC's successes and passionately support EPC incorporating the following components in its roadmap for future work:

1 Fostering honest dialogue between patients and members of their care teams—even, and perhaps especially, when the answer is, "I don't know."

Ms. Roberts highlighted "Let's Reset" as a valuable tool for both patients and providers to "communicate more effectively with the team to make sure that we avoid infections." Let's Reset is a technique developed by NTDS that empowers patients to express criticism or concern to their caregivers without fear of reprisal.

Dr. Gee noted that before the creation of the DKD-C Task Force, the patient perspective was not heard. Working with the task force empowered his advocacy to go into the community and explain to other patients the impact of unmanaged diabetes and to highlight new therapies, such as glucagon-like peptide-1 receptor (GLP1) agonists. He now encourages other patients to talk to their primary care physicians, nephrologists, or transplant teams about new therapies.

Ms. Taylor applauded the efforts of EPC in its groundbreaking work to provide information to patients during the COVID-19 pandemic and to assist with securing priority vaccination for patients. Added Ms. Roberts, "ASN reached out and included me as a patient on that committee. That was really important because it helped ensure that the patient voice was always present." She highlighted the value of ASN's many COVID-19-related webinars available to the public and noted that they became a trusted resource for patients as well.

During the pandemic, patient advocates perceived a new vulnerability in physicians being willing to say, "I don't know." Ms. Roberts believes this has gone a long way toward rebuilding trust that had been lost. "COVID may turn out to be a real benefit to our community, because it has given doctors a way to say that science is messy. COVID has shown that things change rapidly; we learn new things, so we do new things," she said. "I think that will build a culture in the kidney community so patients and physicians can speak together more effectively."

There are so many lonely people who don't have advocates, and they don't even know where to start to ask for help.

—Marla Levy

2 Development of education that meets patients "where they are."

All four patient advocates feel strongly that there is a wide area of opportunity open to EPC to reach those patients who have not yet learned, or had the opportunity, to advocate for themselves.

As Ms. Taylor explained, "My concern is: What about the patients in the facility who don't have this opportunity? We need to make sure their voices are heard and amplified. To empower patients, you have to educate them at their level. I would love to see EPC continue education. We know that kidney disease is rising at an incredible rate in Black, Indigenous, and people of color; a lot of that can be potentially curbed by preventative care, making sure that you educate people about getting kidney screenings …We need to talk about eating right and exercise before, so they never get hypertension or diabetes, or if they do, they know what to do to take care of themselves. That will decrease the number of people on dialysis, which is what we all want. So, let's be more proactive about prevention. Make sure people have the education and the resources to take care of themselves." This philosophy supports outreach to patients with chronic kidney disease (CKD).

Dr. Gee emphasized that along with the patient's voice, social determinants, with all the connections and context that are so critical, must be considered. He recommended, "If you've never been impacted by food apartheid, by transportation issues, by environmental disparities, the only way that science can understand what human suffering really is, is to meet folks in their homes [and] in their communities. To break down barriers, we need to go into these communities unified…focusing on human beings. If we are consistent in that effort, then all of the projects of EPC can consistently improve future outcomes."

When folks get diagnosed with a chronic illness, you get shamed…Nobody asks you how you're doing, nobody asks if you want to seek counseling [or if] you want me to talk to your family...and that's traumatic…You have to learn to understand [that] this machine is my only means of living. Nobody said, 'There's hope.'

—Patrick O. Gee, PhD, JLC

Part of meeting patients where they are includes inviting patients to be a part of the larger process. Clinical trials offer this opportunity. Ms. Roberts stated, "I would like to see physicians ask patients if they're interested in clinical trials… After being diagnosed with kidney disease in 1972, yesterday was the first time a doctor ever asked me if I wanted to participate in a clinical trial. I think that's egregious."

3 Acknowledgment of the medical trauma that often comes with the diagnosis of a chronic illness.

The pain of learning about, and how to deal with, a frightening diagnosis is often overlooked in the rush to provide life-saving treatment. Yet impressing upon care team members the importance of understanding—and acknowledging—this stress on patients may be one of the most critical areas of education that EPC can provide to clinicians.

People don't understand…when you get diagnosed with CKD or ESKD [end stage kidney disease], the life that you wanted doesn't quite happen anymore. And you have to figure out how to mourn and deal with those losses….I'm stuck in this chair, and I feel like I can't get up and move and be a world-changer. I am sad. I am heartbroken. I am disappointed. And there's nothing I can do about it. Because if I don't [do dialysis], I'm gonna die.

—Quin Taylor, BCPA

4 Engagement on a human level.

Above all other points, the patient advocates call on EPC to stress to physicians that the most important component of patient care is acknowledging the patient as a human being.

Advocates note that the patient-physician relationship can take a huge step forward with a few spoken words. As Ms. Levy notes, "When you feel more comfortable with your doctor, this can open the door to sharing very important information you normally wouldn't share. It can be as simple as asking, 'Are you okay?'"

Overlooking engagement can have a profound impact on patients. Ms. Levy, whose experience with AKI involved life support and repeated attempts at outpatient dialysis, explained, "I have a wealth of knowledge…and no one's ever asked me to speak; I've begged to speak at grand rounds, to patients; no one's interested."

Dr. Gee offered his vision for a culture of humility, where patients and providers are each respected for what they offer to the care experience. He challenged providers to consider, "How do you manage all this power that you have and yet, do it in a way that you're humble, and you get to know your patient[s] before their disease state… this breaks down barriers of trust, by asking simple questions...Be a human being."

Moving forward, EPC will build on its projects' successes, embracing the unfiltered patient voice, guided by the four key approaches outlined here. As Ms. Roberts summarized, "No matter what the future is, [patients] are central to that experience." ■

Bonnie Freshly, MEd, CMP, is the Excellence in Patient Care Senior Project Specialist with ASN. Susan Stark is ASN Vice President for Excellence in Patient Care.

The authors would like to thank the following individuals and organizations for their efforts on behalf of EPC:

- Patrick O. Gee, Sr., PhD, JLC; Marla Levy; Glenda Roberts; and Quin Taylor, BCPA
- Alan S. Kliger, MD, Chair, EPC Advisory Committee
- Kristina Bryant, MD, Chair, NTDS
- Members of AKINow, DKD-C Task Force, HDP, AIP, TDAT, and EPI.

Excellence in Patient Care Initiatives

EPC website: https://epc.asn-online.org/
EPC on Twitter: @AsnEpc

NTDS

- Online learning module: "Let's Reset: A New Approach to Empower Patients to Speak Up about Dialysis Safety and Prevent Infection"
- Human factors: Year 2 summary of findings of observations in two outpatient dialysis facilities
- Pilot study: Patient observations of hand hygiene and catheter care for infection control
- Project Firstline: Collaboration with the Centers for Disease Control and Prevention and the American Medical Association to develop four short videos for frontline health care personnel in the outpatient dialysis setting
- Online learning module: Optimizing Hemodialysis Vascular Access Planning
- Online learning module: Antibiotic Prescribing in the Outpatient Dialysis Setting
- "Targeting Zero Infections": Micro-webinar series for fellows, focusing on infection prevention as a new medical director, considerations for infection prevention in water systems, and survey readiness

DKD-C

- Online learning module: Management of Chronic Kidney Disease in People with Diabetes
- Support of US Preventive Services Task Force's consideration of screening for CKD as a preventive service
- Business case: How large corporations can experience cost savings through implementation of new therapies early in the course of kidney disease
- Policy action plan, including access to medications, screening, and prevention

COVID-19 Response Team

- Online learning module: COVID-19 Toolkit for Nephrology Clinicians: Preparing for a Surge
- Online learning module: Pursuing Mental Wellness: The Impact of COVID-19 on Dialysis Facility Staff
- COVID-19 Roundtable: New Therapeutics
- Online learning module: COVID-19: Lessons from the Kidney Community
- Online learning module: Leadership in Uncertainty & Crisis

AKINow

- Journal Club: A new forum for open discussion of relevant papers in kidney journals
- Kidney data warehouse: Interactive molecular database
- Literature review to determine gaps in knowledge about AKI
- Survivorship care plans to record AKI-focused treatment history and plan for follow-up care
- Outreach to other specialties (i.e., cardio-renal) to educate about AKI

Kidney Week events

- "A Look in the Crystal Ball: COVID-19 and the Future of Outpatient Dialysis"
- "The Patient Journey with Diabetic Kidney Disease"
- AKINow: "Leveraging Data Science to Improve Kidney Health"

ASN Home Dialysis Task Force

By Jeffrey Perl, Edward Gould, Ryan Murray, and Bonnie Freshly

The Executive Order on Advancing American Kidney Health, signed in July 2019, included a directive for "a payment model to evaluate the effects of creating payment incentives for greater use of home dialysis and kidney transplants for Medicare beneficiaries on dialysis" (1).

Recognizing this catalyst for change and embracing the expansion of choice in kidney replacement therapy for people with kidney diseases and the need to deliver high-quality home dialysis care, in July 2021, ASN launched the Home Dialysis Task Force.

The task force, co-chaired by Edward Gould, MD, FASN, and Jeffrey Perl, MD, has seated three working groups to expand the use of and access to home dialysis through continuing education and development, training and fellowship, and policy and advocacy. Together, these working groups aim to improve awareness and outcomes of home dialysis therapies by enhancing the education of nephrologists, kidney care professionals, and trainees; addressing disparities in access to home dialysis; and advocating for policies that improve access to all dialysis treatment options in order to promote the highest quality of care.

To inform its early work in the area of training and fellowship, a survey, designed by Yuvaram N. V. Reddy, MBBS, MPH, FASN, was administered to division chiefs and training program directors to quantify:

- the extent of home dialysis training that fellows receive during their fellowship
- the perceptions on requirements needed by programs for competency in home dialysis
- the ability for programs to meet certain threshold requirements

Results of this survey, in combination with an early focus group session, led ASN Council to approve the task force's recommendation that ASN develop and curate an online platform of educational resources and support a weekend training course and longitudinal mentorship program for fellows.

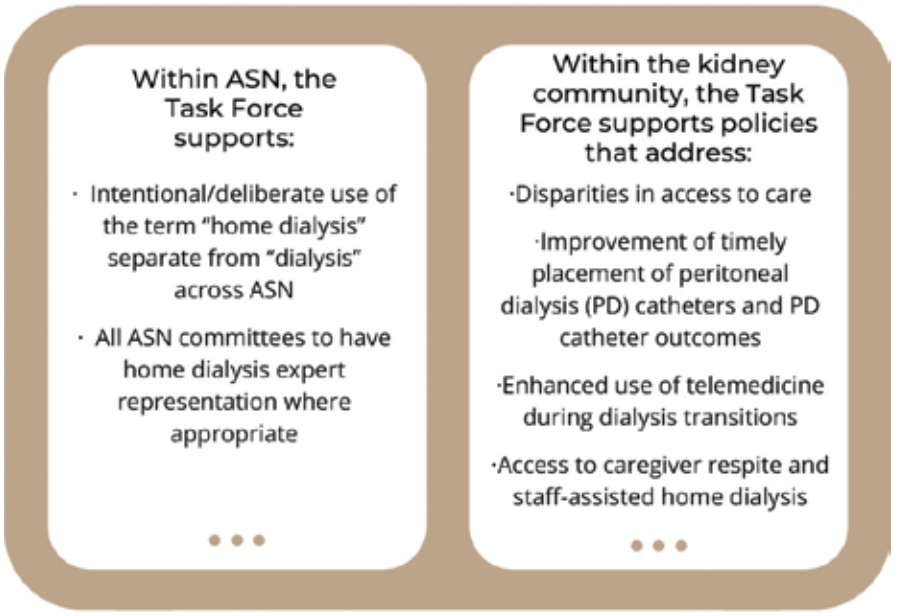
Continued on page 58 >

ASN Home Dialysis Task Force

Continued from page 57

The task force's aims in the arenas of policy and advocacy offer recommendations for both ASN and the broader kidney community. These aims and initiatives will be further outlined in a perspectives piece, which will soon be submitted to a peer-reviewed journal and will describe in depth the task force's efforts in four key areas (see infographic).

The Home Dialysis Task Force recently promoted these concepts and other actions that support enhanced education for home dialysis use to the ASN Task Force on the Future of Nephrology.



Jeffrey Perl, MD, is with St. Michael's Hospital, University of Toronto. Edward Gould, MD, FASN, is with Vanderbilt University Medical Center. Ryan Murray is ASN Senior Manager of Policy and Government Affairs. Bonnie Freshly, MEd, CMP, is Excellence in Patient Care Senior Project Specialist with ASN.

Dr. Perl reports receiving honoraria from Baxter Healthcare USA/Canada, DaVita Healthcare partners, Fresenius Medical Care, DCI, AstraZeneca, and US Renal Care. Dr. Gould reports research funding from Oxthera, Bayer, AstraZeneca, Allena, and Palladio.

Reference

1. Advancing American Kidney Health. *Federal Register,* July 15, 2019. Executive Order 13879 of July 10, 2019. https://www.federalregister.gov/documents/2019/07/15/2019-15159/advancing-american-kidney-health

Transforming Dialysis Access Together

By Vandana Dua Niyyar, Prabir Roy-Chaudhury, and Shane B. Perry

ASN's Excellence in Patient Care is expanding the efforts that the Nephrologists Transforming Dialysis Safety (NTDS) Vascular Access Workgroup began in 2016 through a new initiative, Transforming Dialysis Access Together (TDAT). TDAT's scope will optimize dialysis access care, including peritoneal dialysis and hemodialysis. This initiative will be multifaceted and crosscutting along the spectrum of dialysis access care.

ASN has recruited thought leaders in dialysis access, including patients, nephrologists, interventionists, radiologists, surgeons, training program directors, technicians, and nurses, to provide leadership and content expertise across five key domains. Domain goals include:

Domain 1

TDAT will seek opportunities to establish multidisciplinary partnerships to leverage consensus statements, clinical practice guidelines, innovative techniques, and related initiatives to optimize and improve dialysis access care, especially in assessing access maturation, cannulation, or connection and in reducing errors, infections, and complications.

Domain 2

TDAT will develop educational curricula incorporating the fundamentals of dialysis access into nephrology fellowship training programs utilizing regional educational programs, "train-the-trainer" formats, and virtual and in-person didactic sessions.

Domain 3

TDAT will expand continuing educational programs through novel educational opportunities focused on dialysis access and seek to develop a "one-stop-shop" platform that is interactive, case based, and supportive of skills assessment and improvement.

Domain 4

TDAT will advocate for dialysis access through the establishment of regulatory and legislative priorities in partnership with ASN policy initiatives, the US Food and Drug Administration Center for Devices and Radiological Health, Centers for Medicare & Medicaid Services (CMS) Transitional Add-on Payment Adjustment for New and Innovative Equipment and Supplies, CMS Transitional Drug Add-on Payment Adjustment, and CMS Medicare Coverage of Innovative Technology, among others.

Domain 5

TDAT will address and accomplish dialysis access justice, equity, diversity, and inclusion by advocating for more significant federal and private investments in determining the reasons for the imbalance among underrepresented racial and ethnic groups, ensuring appropriate inclusion of these underserved communities in clinical trials, and developing a framework for dialysis access care equity.

We look forward to sharing updates as the initiative gets underway.

Vandana Dua Niyyar, MD, FASN, FNKF, FASDIN, is a professor of medicine in the Division of Nephrology at Emory University, Atlanta, GA, and has been designated Eminent Physician in the Emory Department of Medicine. Prabir Roy-Chaudhury, MD, PhD, FASN, is a professor of medicine and co-director of the University of North Carolina Kidney Center, Chapel Hill. Shane B. Perry, BS, is the ASN Adult Immunization Project Manager.

Dr. Niyyar reports receiving honoraria or funding from Eversana (BD), Elsevier ClinicalKey, and Medtronic AV Access Webinars. Dr. Roy-Chaudhury reports receiving funding from the National Institutes of Health Small Business Grants as a multiple principal investigator and site principal investigator with Inovasc LLC, Adgero, Cylerus, and Eko and receiving honoraria from W.L. Gore, Medtronic/Covidien, BD-Bard, CorMedix, Humacyte, Akebia, Vifor-Relypsa, Bayer, Reata, Chugai Pharmaceutical, and inRegen. He has ownership interest in Inovasc LLC and is the chief scientific officer and founder. Mr. Perry reports no conflicts of interest.

2022 Scientific Exposition

November 3 – 5

Exhibits and Posters

Orange County Convention Center
West Building, Hall D
9:30 a.m. – 2:30 p.m. daily

Highlights Include:

- Over 150 Exhibiting Companies
- ASN Communities Lounge
- Career Fair
- Complimentary Refreshment Breaks
- Exhibitor Spotlights
- FIT Bowl
- Poster Sessions
- Welcome Reception
- Wi-Fi Service

Welcome Reception

Thursday, November 3, 6:00 – 7:00 p.m.
ASN welcomes you to Orlando, FL with a reception in the exhibit hall the evening of Thursday, November 3.

Support provided by FRESENIUS MEDICAL CARE RENAL PHARMACEUTICALS

Communities Lounge – Booth 1741

A focal point of your exhibit hall experience, visit the lounge to learn more about ASN Communities online forum, meet the leaders, network with your peers, and unwind at the relaxation zone.

FIT Bowl 2022

Stop by and watch teams test their knowledge against their peers. The Fellows-In-Training (FIT) Bowl is a two-day, single elimination tournament held in Hall D of the exhibit hall. Seating is limited.

Thursday, November 3	
10:30 a.m. – 12:30 p.m.	**Elimination Rounds**
Friday, November 4	
10:30 – 11:30 a.m.	**Semi-Finals**
11:30 a.m. – 12:30 p.m.	**Finals**

Support provided by CHINOOK THERAPEUTICS

Exhibitor Spotlight Schedule

Join your colleagues for the latest advances in nephrology practices, products, services, and technologies presented in two theaters on the exhibit hall floor (no continuing education credit). Seating is limited and available on a first come, first served basis. **All presentations include breakfast or lunch.**

Thursday, November 3

10:00 – 10:45 a.m. — **Theater 1**

Jardiance® (empagliflozin) tablets: EMPEROR Clinical Trials Data Subgroup Analyses

Presented by Boehringer Ingelheim | Lilly

11:30 a.m. – 12:15 p.m. — **Theater 2**

The Cardiorenal Connection: Providing Dual Cardiorenal Risk Reduction for Patients with CKD Associated with T2D

Presented by BAYER

12:30 – 1:15 p.m. — **Theater 1**

Are You Thinking Genetic? The Emerging Role of Genetics in CKD

Presented by natera

1:00 – 1:45 p.m. — **Theater 2**

Perspectives on OmniGraf Use in Clinical Practice

Presented by eurofins | Transplant Diagnostics

Friday, November 4

10:00 – 10:45 a.m. — **Theater 1**

Understanding the Complexity of Patients with CKD: Implications for Management

Presented by AstraZeneca

11:30 a.m. – 12:15 p.m. — **Theater 2**

New Data on an Autosomal Dominant Polycystic Kidney Disease (ADPKD) Treatment Option

Presented by Otsuka America Pharmaceutical, Inc.

12:30 – 1:15 p.m. — **Theater 1**

Developing Precision Medicines for Patients with IgAN

Presented by CHINOOK THERAPEUTICS

1:00 – 1:45 p.m. — **Theater 2**

The Importance of Achieving a Complete Response in Lupus Nephritis

Presented by Aurinia

Saturday, November 5

10:00 – 10:45 a.m. — **Theater 1**

Physician-Patient Discussion: Does Patient Care Need to Evolve for Anemia of CKD?

Presented by GSK Medical Affairs

11:30 a.m. – 12:15 p.m. — **Theater 2**

Surveillance Tools and Molecular Innovation for Transplant Patients

Presented by CareDx

12:30 – 1:15 p.m. — **Theater 1**

The Phosphorus Management Puzzle and Need for New Pieces: The Patient and Physician Perspective

Presented by ardelyx

1:00 – 1:45 p.m. — **Theater 2**

First Steps for Females with *GLA* Variants Detected by Kidney Disease Panels: Actionable Findings

Presented by sanofi

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ASN American Society of Nephrology — $6,500,000

American Renal Associates An Innovative Renal Care Company — $1,000,000

Amgen — $1,000,000

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Every dollar gets us one step closer to eradicating kidney diseases.

Join us in funding the cure. Visit www.kidneycure.org or use your phone's camera to scan the QR code.

ASN Joins Medical Specialty Societies in Focus on Adult Immunization

By Rebecca Schmidt and Shane B. Perry

ASN is partnering with the Council of Medical Specialty Societies and the Centers for Disease Control and Prevention (CDC) in the Adult Immunization Project (AIP). ASN is one of seven medical specialty societies participating in the project. (A full list of society project participants can be found in Figure 1.)

Figure 1. Adult Immunization Project society participants

There are several goals of the AIP, including improving the adoption of CDC's Standards for Adult Immunization Practice (SAIP) in nephrology and increasing immunization rates of COVID-19, influenza, and routine vaccinations among patients with kidney diseases. (A full list of all project goals can be found in Figure 2.)

The project started in the fall of 2021 and will continue through September 2026. In September 2023, ASN will partner with seven dialysis corporations and engage with at least 14 dialysis facilities from across the United States.

ASN identified the following vaccine types as having the best opportunity to improve safety within the kidney community and will consider other routine immunizations recommended by the AIP Task Force:

- COVID-19
- Influenza
- Pneumococcal
- Hepatitis B
- Shingles

Figure 2. Adult Immunization Project summary

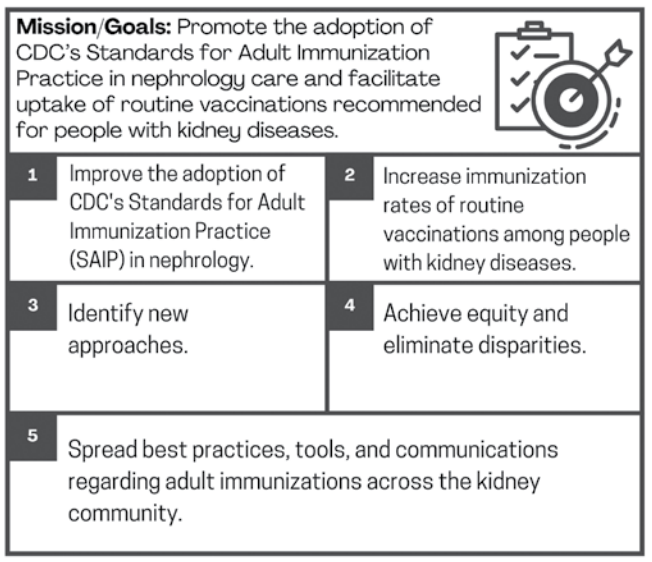

Figure 3. Adult Immunization Project scope

As partnering societies, corporations, and facilities begin this project, the focus will be on increasing COVID-19 and influenza immunization rates. In 2024, the scope will expand to include other immunizations (Figure 3). ASN identified six strategies to achieve the goals of this project:

1) Leadership

ASN seated an AIP Task Force to provide strategic guidance for this project. The task force is composed of nephrology leaders, immunization experts, and health equity champions. Membership on the ASN AIP Task Force will expand to include representatives from dialysis corporations participating in the project. The current membership of the ASN AIP Task Force includes:

- Rebecca Schmidt, DO, FASN, West Virginia University, Chair
- Shuchi Anand, MD, Stanford University
- Marshia Coe, RN, Health Systems Management
- Junichi Ishigami, MD, MPH, Johns Hopkins University

Additional members with diverse expertise in the care of people with kidney diseases will be recruited to join the task force.

2) Engagement

ASN will host quarterly Learning and Action Network (LAN) sessions with the staff of participating dialysis facilities and corporations. The AIP LAN will follow the Institute for Healthcare Improvement Breakthrough Series Collaborative Model. The purpose of the LAN is to promote the sharing of challenges, knowledge, resources, and strategies to facilitate iterative process changes and achieve improved outcomes.

3) Resource Library

ASN curated a compendium of currently available materials, events, and news on the AIP webpage (https://epc.asn-online.org/projects/aip/). Additional materials will be developed and posted to meet the educational and resource needs of kidney patients and professionals.

4) On-Demand Learning

ASN will create kidney patient-focused quality education and "train-the-trainer" materials for professionals who meet the language, accessibility, and adult-learner expectations in a module-based learning management system.

5) Continuous Quality Improvement

ASN will adapt the Assessment, Feedback, Incentive, and eXchange (AFIX) approach for continuous quality improvement. This approach was developed by the CDC to support improvements in vaccination data collection, results/reporting, policy adoption, and communications for professionals and patients.

6) Spread

ASN will contribute to dialysis facility initiatives, staff training, and patient education through immunization-focused messaging, activities, and engagement. Change champions and early adopters will be identified, and best practices will be communicated broadly throughout ASN. Learning modules will be shared to support and sustain growth in immunization practice improvements and vaccine acceptance.

ASN is excited to share the AIP with you. If you have any questions or suggestions for potential quality improvement interventions or immunization resources for kidney patients and professionals, feel free to contact Shane Perry, AIP manager, at sperry@asn-online.org.

Rebecca Schmidt, DO, FASN, is assistant dean of Outreach and Community Engagement and vice chair, Rural Outreach and Service to the State for the Department of Medicine, West Virginia University School of Medicine, Morgantown. Shane B. Perry, BS, is the ASN Adult Immunization Project Manager.

Dr. Schmidt has received research funding from the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; Retrophin (now Travere Therapeutics); and Arbor Research. Mr. Perry reports no conflicts of interest.

The ASN AKINow Initiative: Defining Excellence in the Prevention and Care of Patients with Acute Kidney Injury

By Jorge Cerdá, Samir M. Parikh, Jay Koyner, Anitha Vijayan, and Erin Barreto, on behalf of the AKINow initiative

In hospitals and in the community, the incidence of acute kidney injury (AKI) is high and rising worldwide. At the societal level, AKI is increasingly recognized as a major public health burden (1). For the individual patient, severe AKI is a life-altering event with profound immediate and future consequences. Recently, the COVID-19 pandemic has highlighted the impact of AKI in hospitalized patients with SARS-CoV-2 infection.

Woven through all educational efforts is the acknowledgment that patients and their families are an intrinsic part of the recognition and healing process.

AKI is not a single disease but a syndrome caused by multiple mechanisms in patients with different comorbidities and several potential treatment targets. By developing the AKINow initiative, ASN is committed to defining excellence in AKI prevention and care, aiming to describe pathogenic mechanisms, transform management, reduce morbidity and mortality, and improve short- and long-term outcomes (2).

To achieve these goals, AKINow has established four workgroups that will design a broad educational program, bridging the continuum from basic investigations to clinical studies and focusing on early recognition, intervention, and effective therapies with a patient-centered focus (Figure 1).

The **Public Awareness and Education Workgroup** leverages existing educational platforms and develops novel educational tools for health professionals and patients. This workgroup launched the interactive AKINow Compendium, a searchable database of AKI-related resources within the ASN library of offerings. Further goals of the workgroup include the promotion of AKI quality initiatives, emphasizing the role of continuous quality improvement to enhance AKI recognition and care (3). These initiatives extend not only to the nephrology community, but importantly, they aim to expand into all domains of clinical practice by interacting and developing new knowledge together with all medical and surgical specialists, understanding that AKI recognition and management often rest on non-nephrology practitioners. Woven through all educational efforts is the acknowledgment that patients and their families are an intrinsic part of the recognition and healing process.

The focus of the **Basic Science: AKI-Specific Early Interventions Workgroup** is broad, spanning molecular and cell biology research to investigator education. The group will pursue goals to promote collaborative and inclusive discovery research that translates more effectively to patients, including:

- Developing a centralized, searchable database portal that provides a resource for the research community
- Lowering entry barriers for researchers interested in AKI by developing interactive educational content
- Promoting greater collaboration among AKI basic researchers, translational investigators, and researchers in other fields
- Articulating a preclinical roadmap that facilitates the translation of new discoveries to novel therapies
- Enhancing communication around AKI innovation by fostering an open and vibrant community of patients, researchers, clinicians, and other stakeholders to promote a culture of continuous innovation

The **AKI Recognition and Clinical Interventions: Artificial Intelligence (AI) Workgroup** has outlined objectives in three key domains:

1. Patients. Generate input in designing and implementing fair and equitable AI tools, and identify clinical scenarios based on personal and caregiver experience that could be improved with AI.
2. Clinicians. Incorporate clinician input in the design, value, and implementation of fair and equitable AI tools, and identify clinical uncertainties that may benefit from new AI tools.
3. Researchers. Evaluate current AI processes with a focus on removing implicit bias; develop novel, feasible, and effective AI tools to address gaps identified by patients and clinicians; and develop and implement AI methods with novel sensors for more sensitive assessment of kidney function and injury to advance the science of AKI diagnosis and treatment.

This project, with involvement from a multi-disciplinary group of collaborators, aims to promote efficient and effective use of AI for quality improvement in AKI care, such as the NINJA (Nephrotoxic Injury Negated by Just-in-time Action) program (4).

Specific deliverables include developing risk-stratification and prediction tools; intelligent alert tools; decision support for bundled care compliance; and decision support for implementing pragmatic clinical trials. Importantly, this work will fill gaps to validate available AI tools and to develop new AI tools that do not currently exist, delivering highly useful AI implements for improving AKI care and research and reducing costs.

The **AKI Recovery Workgroup** aims to identify challenges and opportunities to improve post-AKI care (5–7) and to develop tests and supportive strategies that build capacity for delivery of post-AKI care. Research options include a wide spectrum of interventions, spanning the role of the angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, and sodium-glucose cotransporter 2 inhibitors to the importance of physical, mental, and cognitive rehabilitation.

Survivors of AKI are a high-risk, growing population, with potentially poor long-term outcomes. How to care for patients after AKI remains ill-defined and with substantial practice variation. This fall, the workgroup will host two focus group sessions to outline challenges and opportunities in developing evidence-based practice in post-AKI on dialysis care and to determine gaps in care of AKI survivors.

In conclusion

AKI is common, serious, underrecognized, and strongly associated with increased risk of progressive adverse outcomes. Early recognition is essential, and AI improves pattern recognition and awareness, prevention, and management. Developing AKI-specific therapies is indispensable; a better understanding of AKI basic science will lead to the development of effective treatments. Post-AKI recovery care is necessary to alleviate long-term sequelae that severely impact individuals and society. Such efforts will require close interaction and cross-pollination as the most effective pathways to achieve better AKI outcomes, in close collaboration with patients and their families.

During Kidney Week, join AKINow for a Town Hall conversation highlighting the barriers and facilitators to quality care for patients with AKI.

Figure 1. Patient-centered AKI management

AKINow Workgroup members

Chair: Jorge Cerdá, MD, MS, FASN

Public Awareness and Education Workgroup: Jorge Cerdá, MD, MS, FASN – Chair; Guarav Jain, MD, FASN; Marla Levy, Andrew Lewington, MD; Kathleen Liu, MD, PhD, FASN; Etienne Macedo, MD, PhD, FASN; Marlies Ostermann, MD, PhD

Basic Science Workgroup: Samir M. Parikh, MD, FASN – Chair; Anupam Agarwal, MD, FASN; Amandeep Bajwa, PhD; Jorge Cerdá, MD, MS, FASN; Leslie Gewin, MD; Sanjeev Kumar, MD, MBBS, PhD; Sherry Mansour, MD, MS; Mark D. Okusa, MD, FASN

Artificial Intelligence Workgroup: Jay L. Koyner, MD – Chair; Azra Bihorac, MD, MS, FASN; Jorge Cerdá, MD, MS, FASN; Stuart Goldstein, MD, FASN; Kianoush Kashani, MD; Shina Menon, MD; Girish N. Nadkami, MD, MPH; Javier A. Neyra, MD, MS, FASN; Neesh I. Pannu, MD, MS; Karandeep Singh, MD, MS; Danielle Soranno, MD

Recovery Workgroup: Erin Barreto, PharmD, MS, FASN – Co-Chair; Anitha Vijayan, MD, FASN – Co-Chair; Emaad Abdel-Rahman, MD, PhD, FASN; Leslie Gewin, MD; Javier A. Neyra, MD, MS, FASN; Samuel Silver, MD, MS, FASN

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Low-grade Proteinuria in Patients with Systemic Lupus Erythematosus

Are We Missing the Boat for Early Detection of Lupus Nephritis?

By Nasim Wiegley

Lupus nephritis (LN) is a common complication of systemic lupus erythematosus (SLE), occurring in approximately 60% of adults, and is associated with a high degree of morbidity and mortality (1). Currently, the evaluation of kidney involvement in patients with SLE is based on a proteinuria-centric approach. Most guidelines recommend a kidney biopsy for a urine protein-to-creatinine ratio (UPCR) ≥500 mg/g. However, some studies have reported significant inflammatory LN in patients with SLE and even low-grade proteinuria below this threshold (2–5). In a cohort of patients with SLE and isolated proteinuria <1000 mg/g, without active urinary sediment (hematuria), 60% (52 of 87) had histologic evidence of active LN (2). The optimal threshold of proteinuria for early detection of LN remains unclear.

In a recent study in *CJASN*, Wang et al. (6) aimed to evaluate the progression of low-grade UPCR (between 200 and 500 mg/g) to clinically relevant proteinuria. In this observational study of 151 patients with SLE and low-grade proteinuria, 50% (76 of 151) progressed to UPCR >500 mg/g within a short median time of 1.2 years; 61% (46 of 76) were "fast progressors" who reached this state within 2 years of developing low-grade proteinuria. Among the 20 clinically indicated kidney biopsies during the initial 2 years, 80% (16 of 20) showed active LN with subsequent changes in treatment plans.

Risk factors associated with the progression of proteinuria within 2 years of follow-up included low complement levels and a shorter duration of SLE at the index date. Other associated factors included hypertension, diabetes mellitus, younger age, and hematuria.

Complement activation, noted by a decrease in circulating C3 and C4 levels, has long been viewed as an indicator of active LN. In this study, low complement levels had a high sensitivity (82%) and negative predictive value (94%) for progression to overt proteinuria. Monitoring the trend of serum complement levels can be valuable in evaluating patients with SLE and low-grade proteinuria to aid in the early detection of active LN.

The results of this study may warrant a change to our current approach to low-grade proteinuria in SLE. Careful monitoring of urinary sediment and serum complement levels can aid in the early detection of LN and subsequent interventions that reduce long-term complications. Future studies to better understand the underlying pathways of injury and determine biomarkers of early disease are eagerly awaited. ■

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The author reports no conflicts of interest.

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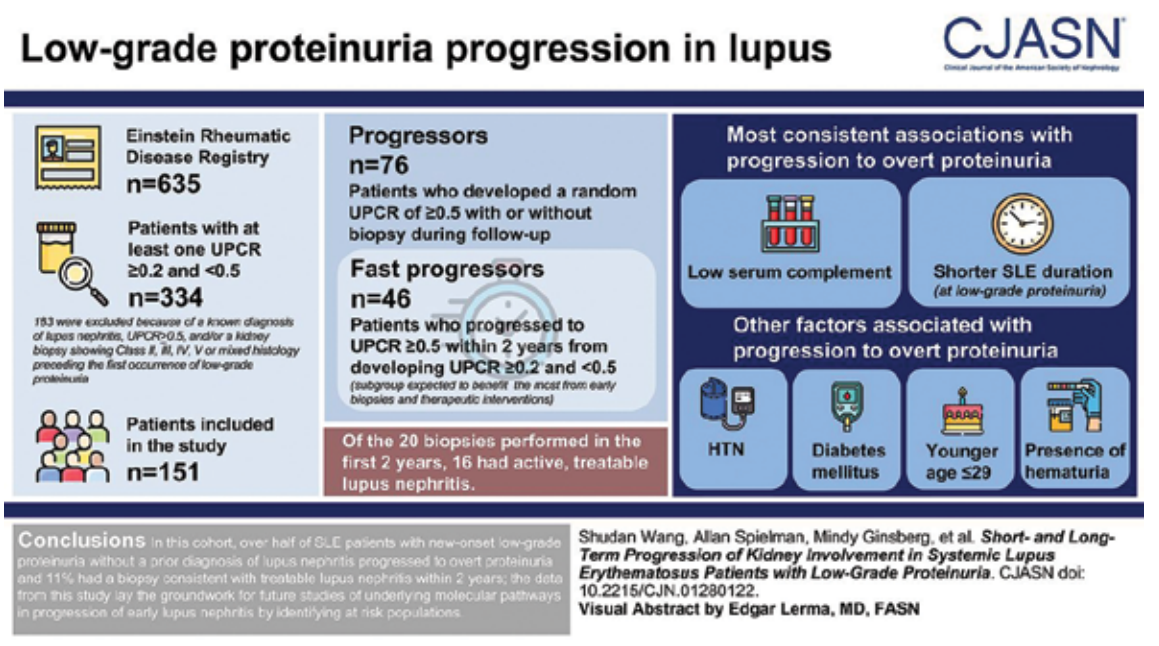

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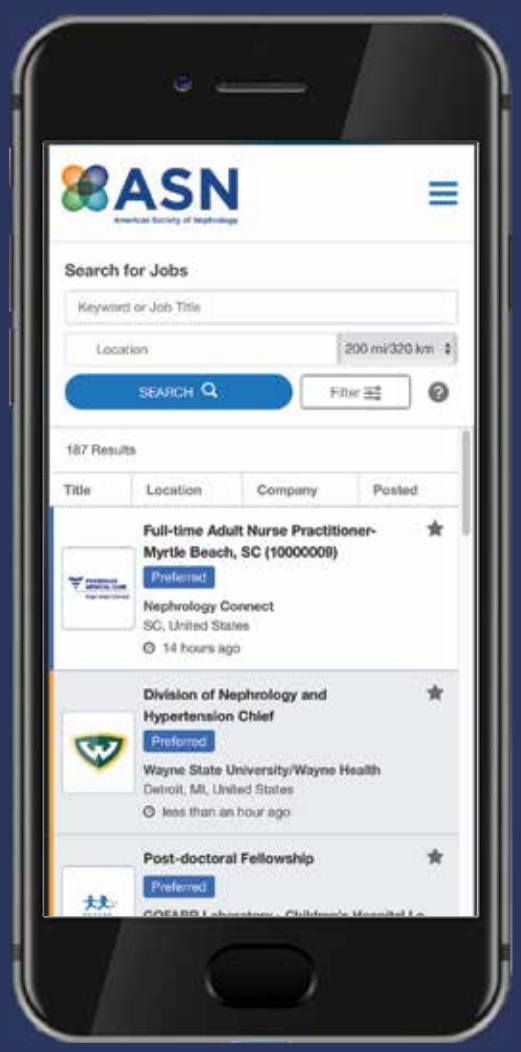

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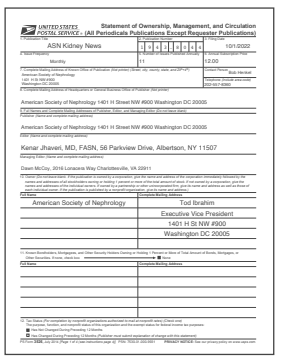

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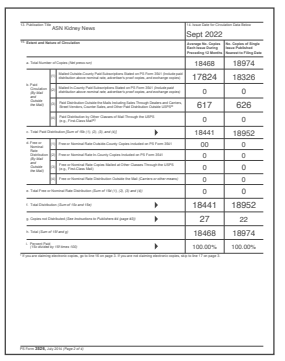

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