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ASN Kidney Health Guidance on Food Additives Offers Tiered Approach

By Bridget M. Kuehn

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Even for highly engaged patients like Sejal Patel, MD, FASN, a nephrologist and two-time kidney transplant recipient and pancreas transplant recipient, managing food additives like potassium and phosphorus in her diet can be challenging. Food additives are not always clearly labeled, and some, like phosphorus, may not be included on the labels at all. "It is really hard because almost everything we eat has those additives," she said. "It is tough to actually measure and figure out how much we are eating in foods."

To help patients and clinicians navigate these challenges, ASN has released a Kidney Health Guidance on Potassium and Phosphorus Food Additives (1). The guidance moves away from traditional, highly restrictive approaches to potassium and phosphorus that left patients feeling that there was little they could eat or that they were unable to follow an overall healthy diet.

Instead, the guidance focuses on managing intake of potassium and phosphorus food additives rather than eliminating whole foods that contain these nutrients. Annabel Biruete, PhD, RD, FASN, cochair of the work group that drafted the guidance and assistant professor in the Department of Nutrition Science at Purdue University in West Lafayette, IN, explained that this shift is in line with growing evidence that potassium and phosphorus food additives are more critical and may have a greater impact on people with kidney diseases than whole food sources of these nutrients.

The guidance also recommends a tiered approach that matches interventions with patients' disease severity as well as their ability and willingness to engage in more intensive dietary interventions. "The ultimate goal is to provide guidance that is hopefully actionable and easy to apply by clinicians and patients depending on their level of involvement, the level of health literacy, [and] their level of willingness to follow complex guidance so that everybody can take something out of it," said work group cochair Csaba P. Kovesdy, MD, FASN, Fred Hatch Professor of Medicine and chief of nephrology at The University of Tennessee Health Science Center in Memphis.

Dietary dilemmas

People living with kidney diseases are at increased risk of developing dangerously high levels of potassium or phosphorus in their blood, making managing levels of these

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Kidney Week Scientific Sessions

THURSDAY

Yes We Can...Cure Kidney Diseases
State-of-the-Art Lecture: Vlado Perkovic, MBBS, PhD, FASN
Clinical Trials Expert Panel: Julie R. Ingelfinger, MD; Alan S. Kliger, MD; and Vlado Perkovic, MBBS, PhD, FASN

Importance of Patient Advocate Partners to Get Discoveries to the Bedside
Celeste Castillo Lee Endowed Lectureship: Bonnie Schneider

Diagnosis and Management of Pregnancy Complications in Glomerular Diseases
Michelle P. Winn, MD, Endowed Lectureship: Michelle A. Hladunewich, MD, MS, FASN

SGLT2 Inhibitor Journey: From Metabolism to Kidney and Heart Protection
Barry M. Brenner, MD, Endowed Lectureship: Ralph A. DeFronzo, MD

Hypertension and Pregnancy
Sharon Silbiger, MD, Endowed Lectureship: Vesna D. Garovic, MD, PhD, FASN

FRIDAY

Systems Biology of Kidney Diseases
State-of-the-Art Lecture: Julio Saez-Rodriguez, PhD
Expert Panel: Laura Barisoni, MD; Matthias Kretzler, MD; Julio Saez-Rodriguez, PhD; and Navdeep Tangri, MD, PhD

Cell by Cell, Space by Space: Unraveling Fibrosis in the Kidney and Heart
ASN-AHA Donald W. Seldin Young Investigator Award: Rafael Kramann, MD, PhD, FASN

ANCA-Associated Vasculitis: Lessons Learned From Patients in Long-Term Remission Off Therapy
Robert W. Schrier, MD, Endowed Lectureship: Ronald Falk, MD, FASN

Challenging the Status Quo in Living Donation: Controversial Medical and Ethical Considerations
Barbara T. Murphy, MB BAO BCh, Endowed Lectureship: Robert S. Gaston, MD

Best Practices for Integrating Race, Ethnicity, and Ancestry in Kidney Care and Research
Christopher R. Blagg, MD, Endowed Lectureship in Kidney Diseases and Public Policy: Keith C. Norris, MD, PhD

SATURDAY

On Kidney Medicine, Drug Development, and Coming Home
State-of-the-Art Lecture: Reshma Kewalramani, MD, FASN

Resilience at Work and at Home: Finding the Rugged Qualities and Collective Resources We Need
State-of-the-Art Lecture: Michael Ungar, PhD

KDIGO Guidelines Decoded: What They Mean for CKD Management in Practice
Garabed Eknoyan, MD, Endowed Lectureship: Ian de Boer, MD, MS

Iron-Induced Hypophosphatemia: A Still Unrecognized Complication of Iron Replacement
Jack W. Coburn, MD, Endowed Lectureship: Myles Wolf, MD, MS, MSc

Delayed Remote Ischemic Preconditioning: Extending the Window for AKI Protection
Burton D. Rose, MD, Endowed Lectureship: Marlies Ostermann, MD, PhD

SUNDAY

Xenotransplantation Advances
State-of-the-Art Panel: David K. C. Cooper, MD, PhD, MA, MS; Paul E. Klotman, MD (moderator); Robert A. Montgomery, MD, PhD; and Leonardo V. Riella, MD, PhD, FASN

Inside

FABHALTA® (iptacopan) 200 mg capsules

To reduce proteinuria in adults with primary IgAN at risk of rapid disease progression (generally a UPCR ≥1.5 g/g)[1]

TAKE ACTION WITH FABHALTA

This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether FABHALTA 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 trial.[1]

Persistent proteinuria despite maximally tolerated RASi ± SGLT2i can signify the need for a different approach[2-4]

In APPLAUSE, a phase 3 clinical trial for adults with primary IgAN and elevated proteinuria, FABHALTA significantly reduced proteinuria at 9 months[1,5]

FABHALTA is a single capsule taken orally twice a day[1]

Scan to explore efficacy and safety data or visit FABHALTA-HCP.com/IgAN

Patient portrayal.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

FABHALTA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life threatening or fatal if not recognized and treated early.

- **Complete or update vaccinations for encapsulated bacteria at least 2 weeks prior to the first dose of FABHALTA, unless the risks of delaying therapy with FABHALTA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.**
- **Patients receiving FABHALTA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS.

CONTRAINDICATIONS

- In patients with serious hypersensitivity to FABHALTA or any of the excipients.
- For initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, or *Haemophilus influenzae* type b.

WARNINGS AND PRECAUTIONS

Serious Infections Caused by Encapsulated Bacteria

- FABHALTA, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis* (caused by any serogroup, including nongroupable strains), and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. The initiation of FABHALTA is contraindicated in patients with unresolved serious infections caused by encapsulated bacteria.
- Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to the start of FABHALTA, according to the current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with FABHALTA. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent FABHALTA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. The benefits and risks of treatment with FABHALTA, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by encapsulated bacteria.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information, including Boxed WARNING on the following pages.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Infections Caused by Encapsulated Bacteria (continued)

- Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Serious infection may become rapidly life threatening or fatal if not recognized and treated early. Consider interruption of FABHALTA in patients who are undergoing treatment for serious infections, depending on the risks of interrupting treatment in the disease being treated.

FABHALTA REMS

- FABHALTA is available only through a restricted program under a REMS called FABHALTA REMS, because of the risk of serious infections caused by encapsulated bacteria.
- Under the FABHALTA REMS, prescribers must enroll in the program; counsel patients about the risks, signs, and symptoms of serious infections caused by encapsulated bacteria; provide patients with the REMS educational materials; ensure patients are vaccinated against encapsulated bacteria; prescribe antibacterial drug prophylaxis if patients' vaccine status is not up to date and treatment must be started urgently; and provide instructions to always carry the Patient Safety Card during treatment and for 2 weeks following the last dose of FABHALTA.
- Further information is available by telephone: 1-833-993-2242 or online at www.FABHALTA-REMS.com.

Hyperlipidemia

- FABHALTA may increase total cholesterol, LDL cholesterol, and serum triglycerides. Some patients required cholesterol-lowering medications.
- Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medications, if indicated.

ADVERSE REACTIONS

- The most common adverse reactions (≥5%) in adults with IgAN receiving FABHALTA were upper respiratory tract infection, lipid disorder, and abdominal pain.

DRUG INTERACTIONS

- Concomitant use of CYP2C8 inducers (eg, rifampin) may decrease iptacopan exposure, which may result in loss of or reduced efficacy of FABHALTA. Monitor the clinical response and discontinue use of the CYP2C8 inducer if loss of efficacy of FABHALTA is evident.
- Concomitant use of strong CYP2C8 inhibitors (eg, gemfibrozil) may increase iptacopan exposure, which may result in an increased risk for adverse reactions with FABHALTA. Coadministration with a strong CYP2C8 inhibitor is not recommended.

USE IN SPECIFIC POPULATIONS

- Because of the potential for serious adverse reactions in a breastfed child, breastfeeding should be discontinued during treatment and for 5 days after the final dose.
- FABHALTA is not recommended in patients with severe hepatic impairment (Child-Pugh class C). No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.

INDICATION

FABHALTA is 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 reduction of proteinuria. It has not been established whether FABHALTA 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.

IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium/glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

References: 1. Fabhalta. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Rovin BH, Adler SG, Barratt J, et al; 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(suppl 4):S1-S276. doi:10.1016/j.kint.2021.05.021 **3.** Medjeral-Thomas NR, Troldborg A, Constantinou N, et al. Progressive IgA nephropathy is associated with low circulating mannan-binding lectin–associated serine protease-3 (MASP-3) and increased glomerular factor H–related protein-5 (FHR5) deposition. *Kidney Int Rep*. 2018;3(2):426-438. doi:10.1016/j.ekir.2017.11.015 **4.** Lim RS, Yeo SC, Barratt J, Rizk DV. An update on current therapeutic options in IgA nephropathy. *J Clin Med*. 2024;13(4):947. doi:10.3390/jcm13040947 **5.** Data on file. APPLAUSE Sub Analysis. Novartis Pharmaceuticals Corp; July 2024.

Please see additional Important Safety Information on previous page and Brief Summary of full Prescribing Information, including Boxed WARNING on the following pages.

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Printed in USA 7/25 FA-11460310

FABHALTA® (iptacopan) capsules, for oral use
Initial U.S. Approval: 2023

BRIEF SUMMARY: Please see package insert for full prescribing information.

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

FABHALTA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b *[see Warnings and Precautions (5.1)]*. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of FABHALTA, unless the risks of delaying therapy with FABHALTA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor. See *Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by encapsulated bacteria.**
- **Patients receiving FABHALTA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS *[see Warnings and Precautions (5.2)]*.

1 INDICATIONS AND USAGE

1.1 Paroxysmal Nocturnal Hemoglobinuria

FABHALTA is indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).

1.2 Immunoglobulin A Nephropathy

FABHALTA is 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 reduction of proteinuria. It has not been established whether FABHALTA 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.

1.3 Complement 3 Glomerulopathy

FABHALTA is indicated for the treatment of adults with complement 3 glomerulopathy (C3G), to reduce proteinuria.

4 CONTRAINDICATIONS

FABHALTA is contraindicated:

- in patients with serious hypersensitivity to iptacopan or any of the excipients.
- for initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, or *Haemophilus influenzae* type b.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Infections Caused by Encapsulated Bacteria

FABHALTA, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria, including *Streptococcus pneumoniae, Neisseria meningitidis* (caused by any serogroup, including non-groupable strains), and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. The initiation of FABHALTA treatment is contraindicated in patients with unresolved serious infections caused by encapsulated bacteria.

Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to administration of the first dose of FABHALTA, according to the current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with FABHALTA. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent FABHALTA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including FABHALTA. The benefits and risks of treatment with FABHALTA, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by encapsulated bacteria.

Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if these signs and symptoms occur. Promptly treat known infections. Serious infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of FABHALTA in patients who are undergoing treatment for serious infections, depending on the risks of interrupting treatment in the disease being treated.

FABHALTA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.2)]*.

5.2 FABHALTA REMS

FABHALTA is available only through a restricted program under a REMS called FABHALTA REMS, because of the risk of serious infections caused by encapsulated bacteria *[see Warnings and Precautions (5.1)]*.

Notable requirements of the FABHALTA REMS include the following:

- Prescribers must enroll in the REMS.
- Prescribers must counsel patients about the risk of serious infections caused by encapsulated bacteria.
- Prescribers must provide patients with the REMS educational materials.
- Prescribers must assess patient vaccination status for vaccines against encapsulated bacteria and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of FABHALTA.
- Prescribers must provide a prescription for antibacterial drug prophylaxis if treatment must be started urgently, and the patient is not up to date with vaccines against encapsulated bacteria according to current ACIP recommendations at least two weeks prior to the first dose of FABHALTA.
- Pharmacies that dispense FABHALTA must be certified in the FABHALTA REMS and must verify prescribers are certified.
- Patients must receive counseling from the prescriber about the need to receive vaccinations against encapsulated bacteria per ACIP recommendations, the need to take antibiotics as directed by the prescriber, and the early signs and symptoms of serious infections.
- Patients must be instructed to carry the Patient Safety Card with them at all times during treatment and for 2 weeks following the last dose of FABHALTA.

Further information is available by telephone: 1-833-99FABHA (1-833-993-2242) or online at www.FABHALTA-REMS.com.

5.3 Monitoring of PNH Manifestations After FABHALTA Discontinuation

In PNH patients, after discontinuing treatment with FABHALTA, closely monitor patients for at least 2 weeks after the last dose for signs and symptoms of hemolysis. These signs include elevated lactate dehydrogenase (LDH) levels along with a sudden decrease in hemoglobin or PNH clone size, fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (such as thrombosis, stroke and myocardial infarction), dysphagia, or erectile dysfunction. If discontinuation of FABHALTA is necessary, consider alternative therapy.

If hemolysis occurs after discontinuation of FABHALTA, consider restarting treatment with FABHALTA, if appropriate, or initiating another treatment for PNH.

5.4 Hyperlipidemia

FABHALTA may increase total cholesterol, LDL-cholesterol, and serum triglycerides *[see Adverse Reactions (6.1)]*.

Of the 54 FABHALTA-treated patients who had a normal total cholesterol level at baseline in APPLY-PNH, 43% developed Grade 1 hypercholesterolemia during the randomized treatment period. One FABHALTA-treated patient in APPLY-PNH experienced increased total cholesterol that worsened to Grade 2 from Grade 1 at baseline.

Of the 34 FABHALTA-treated patients who had a normal cholesterol level at baseline in APPOINT-PNH, 24% developed Grade 1 hypercholesterolemia during the core treatment period.

Of the 60 FABHALTA-treated patients who had LDL-cholesterol ≤ 130 mg/dL at baseline in APPLY-PNH, 17% developed LDL-cholesterol > 130-160 mg/dL, 8% developed LDL-cholesterol > 160-190 mg/dL, and 7% developed LDL-cholesterol > 190 mg/dL during the randomized treatment period. Of the 36 FABHALTA-treated patients who had LDL-cholesterol ≤ 130 mg/dL at baseline in APPOINT-PNH, 11% developed LDL-cholesterol > 130-160 mg/dL and 3% developed LDL-cholesterol > 160-190 mg/dL.

Of the 52 patients with normal triglyceride levels at baseline in APPLY-PNH, 23% developed Grade 1 elevated triglycerides during the randomized treatment period. Three FABHALTA-treated patients in APPLY-PNH experienced an increase in triglycerides from Grade 1 to Grade 2.

Of the 37 FABHALTA-treated patients who had a normal triglyceride level at baseline in APPOINT-PNH, 27% developed Grade 1 elevated triglycerides in the core treatment period.

Of the 102 FABHALTA-treated patients in APPLY-PNH and APPOINT-PNH, two patients required cholesterol-lowering medications.

Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medication, if indicated.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

- Serious Infections Caused by Encapsulated Bacteria *[see Warnings and Precautions (5.1)]*.
- Hyperlipidemia *[see Warnings and Precautions (5.4)]*.

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.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

The data described below reflects the exposure in adults with PNH who received FABHALTA (n = 62) or anti-C5 treatment (US-approved and non-US-approved eculizumab product or US-approved and non-US-approved ravulizumab product, n = 35) in APPLY-PNH [NCT04558918] and adults who received FABHALTA (n = 40) in APPOINT-PNH [NCT04820530] at the recommended dosing regimen for 24 weeks. In APPLY-PNH, serious adverse reactions were reported in 2 (3%) patients with PNH receiving FABHALTA. Serious adverse reactions included pyelonephritis, urinary tract infection and COVID-19. In APPOINT-PNH, serious adverse reactions were reported in 2 (5%) patients with PNH receiving FABHALTA. Serious adverse reactions included COVID-19 and bacterial pneumonia. The most common adverse reactions (≥ 10%) with FABHALTA

were headache, nasopharyngitis, diarrhea, abdominal pain, bacterial infection, viral infection, nausea, and rash.

Table 1 describes the adverse reactions that occurred in > 5% of patients treated with FABHALTA in the APPLY-PNH or APPOINT-PNH studies.

Table 1: Adverse Reactions Reported in > 5% of Patients Treated with FABHALTA in APPLY-PNH or APPOINT-PNH Studies (24-Week Treatment Period)

Adverse reactions	APPLY-PNH		APPOINT-PNH
	FABHALTA (N = 62) n (%)	Anti-C5 (Eculizumab or Ravulizumab) (N = 35) n (%)	FABHALTA (N = 40) n (%)
Headache[a]	12 (19)	1 (3)	11 (28)
Nasopharyngitis[b]	10 (16)	6 (17)	6 (15)
Diarrhea	9 (15)	2 (6)	3 (8)
Abdominal pain[a]	9 (15)	1 (3)	3 (8)
Bacterial infection[c]	7 (11)	4 (11)	2 (5)
Nausea	6 (10)	1 (3)	2 (5)
Viral infection[d]	6 (10)	11 (31)	7 (18)
Arthralgia	5 (8)	1 (3)	0
Thrombocytopenia[a]	4 (6)	0	0
Dizziness	4 (6)	0	1 (3)
Systemic hypertension[a]	4 (6)	0	0
Lipid disorder[e]	4 (6)	0	3 (8)
Rash[f]	2 (3)	0	4 (10)

[a]Includes similar terms.
[b]Nasopharyngitis contains: rhinitis allergic, upper respiratory tract infection, pharyngitis, rhinitis.
[c]Bacterial infection contains: pyelonephritis, urinary tract infection, bronchitis bacterial, bronchitis haemophilus, cholecystitis, folliculitis, cellulitis, arthritis bacterial, sepsis, klebsiella infection, staphylococcal infection, *Pseudomonas* infection, hordeolum, pneumonia bacterial.
[d]Viral infection contains: COVID-19, herpes zoster, oral herpes, nasal herpes, influenza A virus test positive, influenza.
[e]Lipid disorder contains: dyslipidemia, blood cholesterol increased, low density lipoprotein increased, hypercholesterolemia, blood triglycerides increased, hyperlipidemia.
[f]Rash contains: dermatitis allergic, acne, erythema multiforme, rash maculo-papular, rash erythematous.

Clinically relevant adverse reactions reported in less than or equal to 5% of patients includes urticaria in one patient (3%) in APPOINT-PNH.

Description of Select Adverse Reactions (graded per NCI CTCAE Version 4.03 unless noted otherwise)

Platelet Count Decreased
Of the 37 FABHALTA-treated patients who had normal platelet counts at baseline in APPLY-PNH, 43% experienced any Grade thrombocytopenia during the randomized treatment period. Three FABHALTA-treated patients in APPLY-PNH experienced decreased platelets that worsened to Grade ≥ 3 from baseline (one patient with normal platelets that worsened to Grade 4, one patient with baseline Grade 1 that worsened to Grade 4, and one patient with baseline Grade 3 that worsened to Grade 4).

Immunoglobulin A Nephropathy (IgAN)
The safety of FABHALTA was evaluated in APPLAUSE-IgAN, a randomized placebo-controlled, double-blind clinical study in adults with IgAN (eGFR ≥ 20 mL /min/1.73 m^2 at baseline).

The data below reflect FABHALTA exposure in 235 patients with IgAN (eGFR ≥ 20 mL/min/1.73 m^2 at baseline) with a median duration of 43 weeks (up to 104 weeks) in APPLAUSE-IgAN. Table 2 describes the adverse reactions that occurred in ≥ 3 % of patients treated with FABHALTA and were ≥ 2% higher in frequency than placebo. All of these adverse reactions were mild or moderate in severity.

Table 2: Adverse Reactions Reported in ≥ 3% of Adult Patients with IgAN (eGFR ≥ 20 mL /min/1.73 m^2) Treated with FABHALTA and ≥ 2% Higher in Frequency Than Placebo in APPLAUSE-IgAN

Adverse reaction	FABHALTA (N = 235) n (%)	Placebo (N = 235) n (%)
Upper respiratory tract infection	20 (9)	16 (7)
Lipid disorder[1]	15 (6)	10 (4)
Abdominal pain[1]	15 (6)	5 (2)
Nausea	8 (3)	2 (1)
Dizziness	7 (3)	2 (1)

[1] Includes similar terms.

Complement 3 Glomerulopathy (C3G)
The safety of FABHALTA was evaluated in APPEAR-C3G, a randomized, placebo-controlled, double-blind trial in adult patients with native kidney C3G. No new adverse reactions were identified during the 6-month placebo-controlled period of APPEAR-C3G, in which 38 patients were treated with FABHALTA and 36 patients were treated with placebo. The most common adverse reactions that occurred in ≥ 10% of patients treated with FABHALTA and were ≥ 5% higher in frequency than placebo were nasopharyngitis (11% in FABHALTA, 3% placebo) and viral infections (29% in FABHALTA, 22% placebo), mainly respiratory infections. One patient (3%) on FABHALTA and none on placebo had a serious adverse reaction of pneumonia and bacteremia secondary to an encapsulated organism (*S. pneumoniae*).

7 DRUG INTERACTIONS

7.1 CYP2C8 Inducers
Concomitant use of CYP2C8 inducers (e.g., rifampin) may decrease iptacopan exposure, which may result in loss of or reduced efficacy of FABHALTA. Monitor the clinical response and discontinue use of the CYP2C8 inducer if loss of efficacy of FABHALTA is evident.

7.2 Strong CYP2C8 Inhibitors
Concomitant use of strong CYP2C8 inhibitors (e.g., gemfibrozil) may increase iptacopan exposure, which may result in an increased risk for adverse reactions with FABHALTA. Coadministration with a strong CYP2C8 inhibitor is not recommended.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
Available data from clinical trials with FABHALTA use in pregnant women are insufficient to identify 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 untreated PNH, IgAN, or C3G in pregnancy *(see Clinical Considerations)*. The use of FABHALTA in pregnant women or women planning to become pregnant may be considered following an assessment of the risks and benefits.

In animal reproduction studies, oral administration of iptacopan to pregnant rats and rabbits during organogenesis at exposures 4- to 6-times the human exposure (based on AUC) at the maximum recommended human dose (MRHD) of 200 mg twice daily did not induce embryo or fetal toxicity *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of major birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-Associated Maternal and/or Embryo/Fetal Risk
PNH in pregnancy is associated with adverse maternal outcomes, including worsening cytopenias, thrombosis, infections, bleeding, miscarriages, increased maternal mortality, and adverse fetal outcomes, including fetal death and premature delivery.

IgAN 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.

C3G in pregnancy may be associated with adverse maternal outcomes, in particular preeclampsia and miscarriage, as well as adverse fetal outcomes including prematurity and low birth weight.

Data
Animal Data
In an embryo-fetal development study in rats, oral administration of iptacopan during organogenesis did not cause embryo-fetal toxicity when given up to the highest dose of 1,000 mg/kg/day, which corresponds to 4-times the MRHD based on AUC.

In an embryo-fetal development study in rabbits, oral administration of iptacopan during organogenesis did not cause embryo-fetal toxicity when given up to the highest dose of 450 mg/kg/day, which corresponds to 6-times the MRHD based on AUC.

In a pre- and postnatal development study in rats, oral administration of iptacopan during gestation, parturition, and lactation did not cause adverse effects in offspring when given up to the highest dose of 1,000 mg/kg/day, which corresponds to 4-times the MRHD based on AUC.

8.2 Lactation
Risk Summary
There are no data on the presence of iptacopan or its metabolites in either human or animal milk, the effects on the breastfed child or on milk production. Since many medicinal products are secreted into human milk, and because of the potential for serious adverse reactions in a breastfed child, breastfeeding should be discontinued during treatment and for 5 days after the final dose.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients with PNH, IgAN, or C3G have not been established.

8.5 Geriatric Use
There were 29 PNH patients 65 years of age and older in APPLY-PNH and APPOINT-PNH *[see Clinical Studies (14) in the full prescribing information]*. Of the total number of FABHALTA-treated patients during the 24-week treatment period in these studies, 21 (20.6%) were 65 years of age and older, while 7 (6.9%) were 75 years of age and older. There were 8 IgAN patients 65 years of age and older in APPLAUSE-IgAN *[see Clinical Studies (14) in the full prescribing information]*. Of the total number of FABHALTA-treated patients, 3 (2.4%) were 65 years of age and older. Clinical studies of FABHALTA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.

8.7 Hepatic Impairment
The use of FABHALTA is not recommended in patients with severe hepatic impairment (Child-Pugh class C). No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

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KIDNEY WEEK 2025 HIGHLIGHTS

https://doi.org/10.62716/kn.001992025

Exciting, dynamic plenaries daily

The opening plenary on Thursday, November 6, features the ASN President's Address; the State-of-the-Art Lecture "Yes We Can...Cure Kidney Diseases" by Vlado Perkovic, MBBS, PhD, FASN; two featured high-impact clinical trials; and an expert panel including Julie R. Ingelfinger, MD, and Alan S. Kliger, MD.

On Friday, November 7, the plenary features the State-of-the-Art Lecture "Systems Biology of Kidney Diseases" by Julio Saez-Rodriguez, PhD, followed by an expert panel including Laura Barisoni, MD; Matthias Kretzler, MD; and Navdeep Tangri, MD, PhD.

On Saturday, November 8, the plenary features two State-of-the-Art Lectures: "On Kidney Medicine, Drug Development, and Coming Home" by Reshma Kewalramani, MD, FASN, and "Resilience at Work and at Home: Finding the Rugged Qualities and Collective Resources We Need" by Michael Ungar, PhD.

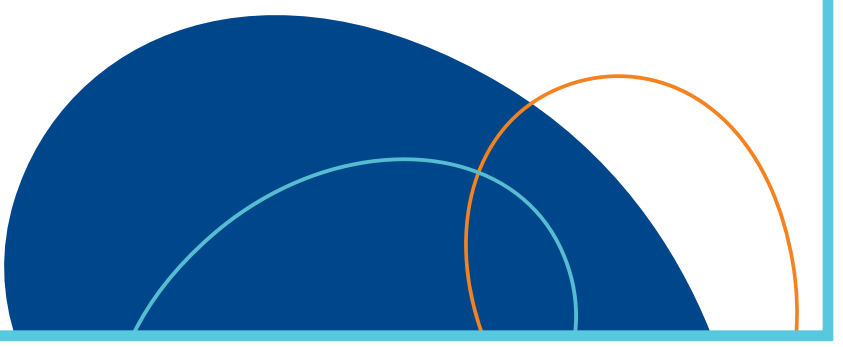
The full plenary on Sunday, November 9, is focused on xenotransplantation, an area that has seen significant advances driven by the organ-shortage crisis and a sustainable alternative to human organ donation. ASN has assembled an expert panel to discuss xenotransplant topics: David K. C. Cooper, MD, PhD, MA, MS; Paul E. Klotman, MD (moderator); Robert A. Montgomery, MD, PhD; and Leonardo V. Riella, MD, PhD, FASN.

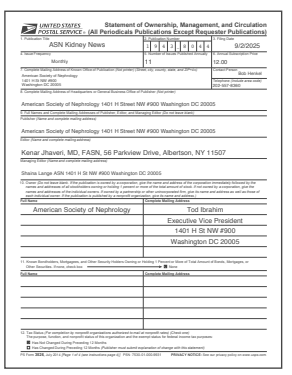
TIME100 Most Influential People 2025

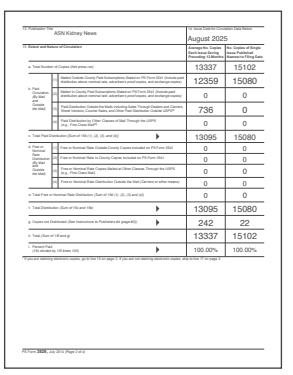
Congratulations to Reshma Kewalramani, MD, FASN, and Robert A. Montgomery, MD, PhD!

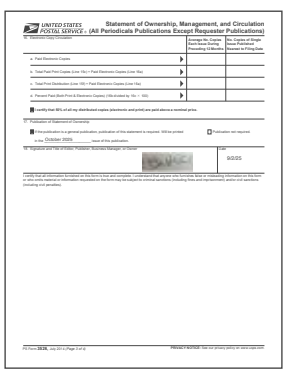
Late-breaking clinical trials

Kidney Week features late-breaking clinical trials that will have significant impact on clinical practice on all topics touching kidney diseases. Two high-impact clinical trials will be featured in the opening plenary, plus multiple late-breaking oral sessions. This year, late-breaking clinical trials have an increased collaboration with *JASN*, *Journal of the American Medical Association*, *The Lancet*, and *The New England Journal of Medicine*.









CORPORATE SUPPORTERS 2025

The ASN Corporate Support Program recognizes supporters year round for their generous contributions to the Society. Through this program, supporters help ASN lead the fight against kidney diseases. ASN gratefully acknowledges the following companies for their contributions in 2025.

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As of September 3, 2025

ASN Kidney Health Guidance

Continued from cover

nutrients critical, according to the guidance. Yet doing so can be a challenge, as potassium and phosphorus additives are nearly ubiquitous in the food supply, especially in processed foods. "It is not easy to navigate this landscape because of the number of [potassium and phosphorus] food additives, the difficulty of identifying them, or the amount of potassium and phosphorus additives in many foods and the variability of an individual's risk when it comes to exposure to these additives," said Kovesdy.

Most of the US population likely consumes too much phosphorus, according to the guidance. Although phosphorus is an essential nutrient, in people with kidney diseases, excess blood levels can lead to calcification of soft tissue and blood vessels and other complications. As a result, limiting dietary phosphorus intake is a pillar of care for people with chronic kidney disease and those on dialysis, in addition to the use of phosphorus-lowering medications, the guidance states.

Limiting phosphorus additives is the most effective way of lowering phosphorus, per the guidance. However, it can be challenging because these additives are so common in many food items. Food labels are not required to list the amount of phosphorus, making it difficult to determine the amount in a serving. Additionally, many phosphorus-containing food additives are not easily recognizable on the ingredient list, Biruete explained.

Managing potassium intake is "trickier," noted Biruete, because high potassium diets can be beneficial to patients with cardiovascular disease, a common comorbidity in people with kidney diseases. In fact, food producers often add potassium additives to foods as a heart-healthy alternative to sodium. Yet, excess blood potassium levels can lead to complications in people with advanced kidney diseases. "When we are telling people not to consume potassium additives, we may be lowering potassium consumption in some people who may benefit," she said. To balance this trade-off, the guidance recommends limiting restrictions on potassium additives to patients at high risk of excess blood potassium levels.

A person's dietary needs also evolve as they progress through different stages of kidney disease, when they initiate dialysis, or undergo a transplant. "That can be overwhelming for patients," said work group member Kelly Lambert, RDN, PhD, an associate professor at the School of Medical, Indigenous and Health Sciences at the University of Wollongong in Australia. "If you are following the wrong diet at the wrong time, there may be negative consequences."

There are also unique challenges for people with comorbid conditions. Patel, who had type 1 diabetes before receiving a pancreas transplant, said she still tries to follow a healthy lifestyle to combat the effects of immunosuppressants that can cause diabetes. She explained that it can be a struggle to balance multiple recommendations or priorities, which may lead to imbalances in electrolytes and metabolic disturbances with just the allografts themselves. Lambert noted that people with comorbid conditions may see multiple specialists, each focused on a single condition in isolation from the others.

"Nobody is really looking at the diet holistically," Lambert said. For example, an individual with type 2 diabetes may be advised to eat a low glycemic index diet to reduce spikes in blood sugar. Yogurt may be a nutritious option, but it also contains a lot of potassium and phosphorus, which can be problematic for people with kidney diseases, she noted.

Right patient, right approach

To help overcome these challenges and promote more nuanced nutrition advice, the work group recommends a tiered approach (Figure). The goal is to avoid pitfalls of overly restrictive approaches that may lead to an unhealthy dietary pattern, a monotonous diet, and stress for patients, Biruete explained. "By creating a tiered approach, we are sensing whether the patient's motivation is adequate, if their education and knowledge are adequate, if the patient has access to a trained dietitian who can work with them on more advanced and intensive strategies," she said. "We are pairing the right patient with the right clinician, with the right tools."

For patients at low risk from these additives or those who clinicians perceive as having low motivation to manage food additives, the work group recommends a balanced diet, with fewer processed foods and lower sodium items that use potassium as an additive as part of their sodium management plan.

Patients with more advanced disease or those who are more motivated may receive food label education on avoiding these additives and demineralization strategies. Those with the greatest need or motivation can work with a renal dietitian on a personalized plan based on their diet. For example, Biruete explained that for someone who eats a lot of packaged foods or desserts, a renal dietitian may recommend limiting consumption of these items, which are often high in phosphorus additives. She acknowledged that it is probably not possible in our current food environment for patients to avoid additives altogether. "We don't want to create a negative approach to all processed foods but really those foods that are not providing a lot of nutrition and that are only providing a lot of additives," she said.

The tiered approach also acknowledges the realities that may limit patients' choices. "People are busy, and they don't always have time to cook from scratch, and they may not be able to afford to eat perfectly, so we have to give sensible advice to people about other food choices that may not be perfect," Lambert said.

Implementation strategies

The goal of the guidance is to create flexible tools that meet both clinicians and patients where they are. That strategy, Kovesdy said, means considering a patient's level of understanding, their culture, their social environment, and their socioeconomic status to develop personalized interventions. "Diet is very personal," Kovesdy explained. "As health care [practitioners], we want to approach things scientifically. But patients approach this as food; it's their everyday life. It affects not just their health but also their social interactions. Some patients have limited access to certain foods."

Lambert noted that a nephrologist may not have time to provide all of the necessary education, but they can provide basic healthy eating advice and refer to a renal dietitian. Dietitians can use the tiered approach to match the right approach to the right patient at the right time.

The guidance also includes a list of tools that clinicians can use to help guide their patients. "Patients will now have advice that enables them to have a wider variety of foods or not feel so guilty about the food choices because we're learning more every year about what is a better choice, what would be the safer choice," Lambert said.

Next steps

The work group acknowledges that the data available on food additives have limitations. The guidance calls for more clinical trials on the health effects of food additives on people with kidney diseases or other common comorbid conditions, as well as clinical trials of additive-reducing dietary interventions.

Additionally, Lambert noted that the food supply is changing rapidly, making it difficult for both patients and clinicians to keep up. She explained that the composition of food products can change, so a staple item that a patient is buying regularly can change and no longer be a good option.

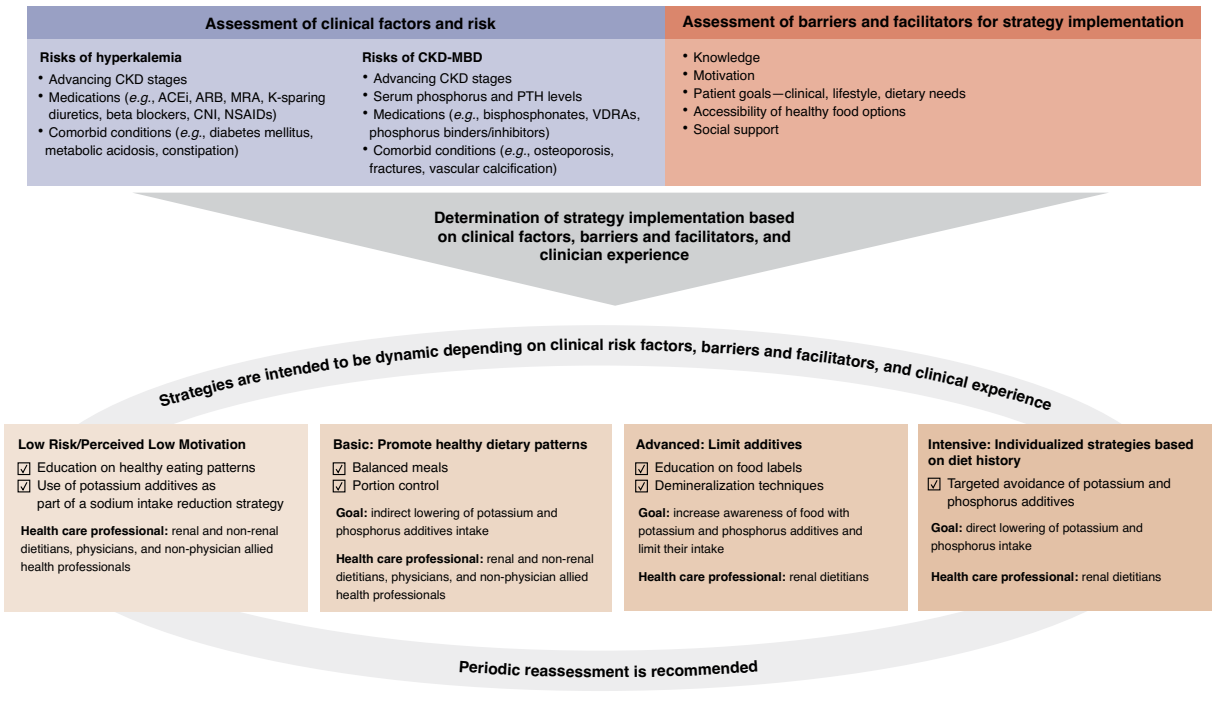
"It is really hard for health professionals and patients to keep on top of what is the right thing to eat," Lambert said. For example, she noted that one of the discussions that the work group had was about "plumping," a technique food producers use to make a piece of meat look bigger or more appetizing by injecting it with a solution. Historically, that has been a sodium chloride solution, but many producers have switched to phosphorus solutions instead in response to recommendations to lower sodium in the food supply.

"[Plumping solutions are] not well-labeled on the packaging unless you know what you are looking for," she said. Lambert noted that even as a dietitian, she finds it exhausting to try to keep up with changes in the food supply—an even more difficult task for patients who are managing a complex health condition and may be tired after dialysis.

Biruete said the kidney health community is ready to collaborate with the US Food and Drug Administration to create easier-to-read food labels or front-of-package information to make managing additives easier for people with kidney diseases. Lambert noted that the work group may also need to revisit the guidance in response to new information or changes in the food supply. But in the meantime, the guidance offers advice to help move the field forward.

"It's the first step in the right direction for helping people understand dietary change," Lambert said. "You just can't do everything all at once. So having a stepped approach at least enables people to make a few steps in the right direction."

Figure. Tiered approach to assessment and intervention



ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CNI, calcineurin inhibitor; MBD, mineral and bone disorder; MRA, mineralocorticoid receptor antagonist; NSAIDs, nonsteroidal anti-inflammatory drugs; PTH, parathyroid hormone; VDRAs, vitamin D receptor activators.

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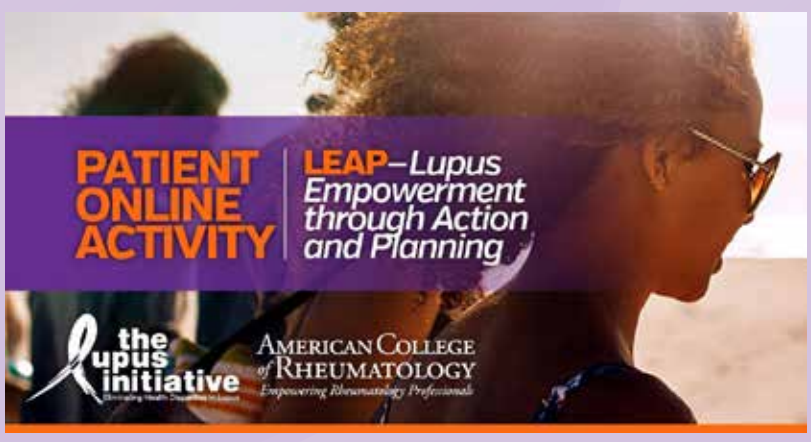

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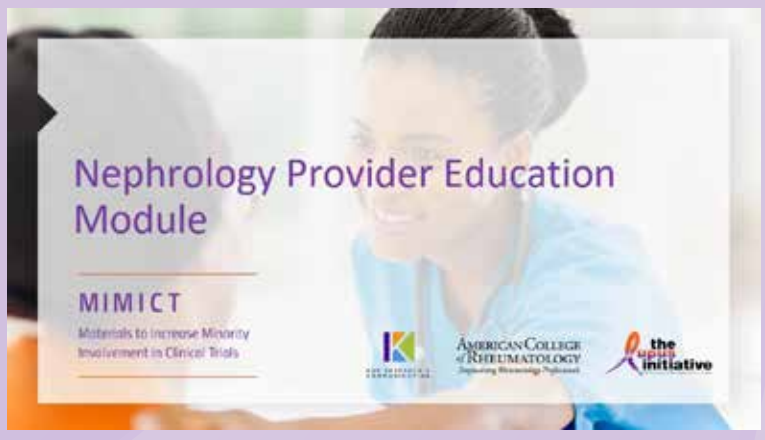

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ASN Executive Vice President's Update

Highlighting Selected ASN Accomplishments in 2025

By Tod Ibrahim

https://doi.org/10.62716/kn.002102025

ASN is committed to transforming kidney care and improving lives through science, education, advocacy, and collective action. Under the leadership of President Prabir Roy-Chaudhury, MD, PhD, FASN, and the ASN Council, the society made significant progress in all of these areas this year while always concentrating on the best interests of the more than 850 million people living with kidney diseases worldwide.

To advance kidney care, ASN:

1. expanded the ASN Diabetic Kidney Disease Collaborative into saving kidneys, hearts, and lives;
2. formed an ASN-European Renal Association (ERA)-International Society of Nephrology (ISN) Task Force on using new pharmacologic therapies to prevent the progression of kidney diseases;
3. released the ASN Glomerular Diseases Collaborative's compendium and published "Barriers to Patients Accessing Specialized Treatment for Glomerular Diseases" (1);
4. published ASN Kidney Health Guidance, "ASN Kidney Health Guidance on the Outpatient Management of Patients With Dialysis-Requiring Acute Kidney Injury," in *JASN* (2);
5. supported the "Acute Kidney Injury (AKI): From Bench to Bedside" conference and The University of Alabama at Birmingham Continuous Renal Replacement Therapy Academy through ASN AKINow;
6. published ASN Kidney Health Guidance in *JASN* highlighting the state of science regarding the effects of potassium and phosphorus additives on people with chronic kidney disease (3);
7. developed an ASN Centers of Excellence in Home Dialysis pilot program;
8. collaborated with the American Medical Association (AMA) and the Centers for Disease Control and Prevention on Project Firstline, which provides infection-prevention training for frontline workers;
9. designed a Multi-Drug Resistant Organisms Compendium;
10. produced an educational video series, defined dialysis access training for nephrology fellows, created a train-the-trainer curriculum, and published "Current State and Future Direction of Vascular Access Training in the United States" (4) through ASN's Transforming Dialysis Access Together;
11. initiated a vaccination campaign through the ASN Kidney Community Vaccination Collaborative;
12. established the ASN Humanitarian Kidney Support Program; and
13. participated in the Global Humanitarian Kidney Support Initiative, a collaboration that also includes ERA, ISN, and Direct Relief, a humanitarian aid organization, active in all 50 states and more than 80 countries (5).

To foster kidney science and innovation, ASN:

1. funded 23 new and 22 continuing grant recipients—at more than $3 million annually—through KidneyCure, ASN's separately incorporated foundation for kidney research;
2. arranged for ASN Kidney Week to present Late-Breaking Clinical Trials during a plenary session for the first time;
3. concluded the term of founding *Kidney360* Editor-in-Chief Michael Allon, MD, and selected his successor, Charuhas V. Thakar, MD, FASN;
4. held the Kidney Innovation Conference, "Innovation Through Collaboration";
5. contributed to both "Looking to the Future: Xenotransplantation and Kidney Regenerative Approaches" at the Kidney Disease Clinical Trialists Workshop and the Alport Syndrome Foundation's Research and Regulatory Workshop to identify opportunities to pursue in catalyzing drug development through the Kidney Health Initiative (KHI);
6. addressed regulatory pathway challenges through KHI, such as a 2024 publication (6) about C3 glomerulopathy that informed the Food and Drug Administration's evaluations and approvals of two drugs in 2025 for this ultrarare kidney disease;
7. pursued projects to address drug development pathways for AKI (7), transplant immunosuppression (8), and sickle cell kidney disease (in collaboration with the American Society of Hematology) through KHI;
8. convened experts to describe a framework for simplifying pediatric clinical trials and organized a Kidney Week session, "Upping Our Game: Advances in Clinical Trials for Pediatric Kidney Diseases," through KHI; and
9. published a toolkit to inform parents who are considering their child's participation in clinical trials, introduced during the virtual meeting, "Making Pediatric Clinical Trials Family Centric," through KHI.

To enhance nephrology education and professional growth, ASN:

1. held the ASN Kidney Tutored Research and Education for Kidney Scholars (TREKS) program in Bar Harbor, ME, and in Chicago, IL;
2. planned the ASN Kidney Students and Residents (STARS) program;
3. provided travel support for trainee members of the American Physician Scientists Association (APSA) to attend the Association of American Physicians/The American Society for Clinical Investigation/APSA joint meeting;
4. supported the ASN Loan Mitigation Program;
5. exhibited at the Student National Medical Association Annual Medical Education Conference and the American College of Physicians Internal Medicine Meeting to generate interest in nephrology careers;
6. continued the Karen L. Campbell, PhD, Travel Support Program for Fellows;
7. offered the William E. Mitch, III, MD, FASN, International Scholars Program;
8. supported travel assistance for the Advances in Research Conference (Early Program): "Generative Artificial Intelligence in Kidney Disease Research and Management";
9. advocated successfully with the American Society of Transplantation for the Accreditation Council for Graduate Medical Education (ACGME) to accredit transplant nephrology training programs;
10. launched the ASN Nephrology Subspecialty Training Database to collate nephrology subspecialty training programs in North America;
11. provided input to the American Board of Internal Medicine (ABIM), which initiated a pilot program to create a path to ABIM board eligibility in internal medicine for international medical graduates who complete an ACGME-accredited fellowship either as an "exceptionally qualified candidate" or as a graduate of an internal medicine training program with ACGME International advanced specialty accreditation;
12. facilitated the ASN In-Training Examination for nephrology fellows;
13. held the ASN Board Review Course & Update;
14. produced the ASN Kidney Self-Assessment Program and the ASN Nephrology Self-Assessment Program; and
15. provided education for the entire kidney care team and offered an estimated 410 hours of continuing education credits to more than 12,000 fellows, nephrologists, nurses, pharmacists, and other professionals.

To assert the value of nephrology to health care, ASN:

1. completed the third year as a member of the AMA Specialty and Service Society, which means that ASN can join the AMA House of Delegates in 2026, making the society eligible to participate in the AMA/Specialty Society Relative Value Scale Update Advisory Committee;
2. provided travel support for 75 nephrology fellows to attend Nephrology Business Leadership University;
3. initiated the ASN Fostering Innovative Leaders in Nephrology and Dialysis (FIND) program;
4. partnered with Columbia University to hold "Nephro-Economics 2025: Advancing Kidney Care in a Changing Environment";
5. offered nephrologists access to compensation and productivity data specific to their specialty and practice situation through the ASN Compensation Tool; and
6. launched the ASN Transplantation Compensation Toolkit Task Force.

To lead kidney health policy and advocacy, ASN:

1. distributed monthly "Dear Colleague" letters on ASN's latest kidney health advocacy efforts, which were organized around the goals outlined in "STAND for Kidney Health":
   - Start earlier to prevent, diagnose, and treat kidney diseases.
   - Transform kidney transplant to expand access to the optimal therapy.
   - Accelerate research, discovery, and innovation to advance American kidney health.
   - Nurture a nephrology workforce to meet patient needs.
   - Drive efficiency to deliver value in kidney health (9);

2. created a website that provides up-to-date information clarifying ASN's efforts to engage "Congress and the Trump Administration, advocating for policies to create transformative changes in kidney health" (10);
3. pursued the establishment of an Officer of Kidney Health and Transplantation at the Department of Health and Human Services;
4. worked with other members of the kidney community—particularly the American Kidney Fund (AKF) and the National Kidney Foundation (NKF)—to demand routine screening for chronic kidney disease in adults who are asymptomatic;
5. joined more than 100 organizations in urging Congress to protect the scientific integrity of the US Preventive Services Task Force;
6. requested that the Centers for Medicare & Medicaid Services (CMS) reverse its decision to remove race and ethnicity questions from Form CMS-2728, the End Stage Renal Disease (ESRD) Medical Evidence Report, in concert with the American Nephrology Nurses Association (ANNA) and NKF;
7. collaborated with Congress on authorizing bills to improve the transplant system;
8. led annual visits to Capitol Hill to bolster transplant funding through appropriations;
9. championed transplant in models from the CMS Innovation Center, particularly the Increasing Organ Transplant Access Model;
10. supported the introduction of bipartisan bills that remove barriers to living donation;
11. supported the National Institutes of Health (NIH)—especially the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)—amid proposed cuts and reorganization;
12. urged Congress to ensure that legally appropriated fiscal year 2025 NIH funds are released;
13. called on Congress to provide $51.303 billion for NIH in fiscal year 2026, including a proportional funding increase of no less than $207 million for NIDDK;
14. agreed to help lead an advocacy campaign organized by Research!America to "educate the public about the critical importance of federal funding for medical and health research at NIH" (11);
15. produced a blue-ribbon report, "Transforming Kidney Health Research" with the American Association of Kidney Patients, AKF, the American Society of Pediatric Nephrology, and NKF;
16. advocated successfully for incoming nephrology residents, fellows, and other trainees to obtain expedited review and processing, considering the pause for issuance and approval of all visas;
17. provided nephrologists with timely information on navigating changing regulations for J-1 and H1-B visa holders;
18. partnered with the Migration Policy Institute to conduct a holistic assessment of international medical graduate nephrologists who represent 50% of the current nephrology workforce;
19. joined forces with ANNA, NKF, and the Renal Physicians Association (RPA) to develop principles for ensuring that the organizations work together to expand, strengthen, and support the dialysis care team;
20. worked with other members of the kidney community, including Kidney Care Partners, to encourage the federal government to reimagine the Medicare ESRD Program bundle; and
21. partnered with the kidney community and other advocates to guarantee access to innovation and data in Medicare Advantage, address data challenges in kidney health (such as accessing affordable data and increasing interoperability in electronic health records), and ensure appropriate quality parameters like measuring longitudinally for the care of all Americans living with kidney diseases regardless of payor.

Throughout 2025, ASN also attempted to unify the kidney community. During the last 4 months of the year alone, ASN met with the RPA leadership, cosponsored "A Day of Collaboration" at the ANNA Nephrology Nursing Summit, continued an annual tradition of holding a joint leadership meeting with ERA and ISN, and cosponsored a half-day session (with the American Nephrologists of Indian Origin) at the 54th Annual Conference of the Indian Society of Nephrology.

ASN will unveil a new strategic plan on January 1, 2026. This plan will help ensure that the society continues to strengthen programs like Kidney Week, initiate new activities, and navigate uncertainty across government and health care next year and beyond. If you are interested in becoming more involved, please contact ASN at email@asn-online.org. ■

Tod Ibrahim, MLA, is executive vice president, American Society of Nephrology, Washington, DC. You can reach him at tibrahim@asn-online.org.

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Journey to Nephrology: Experiences From Pre-Medical Students

By Ghelatia Petros Araia and Natalia Khoshnam

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Ghelatia Petros Araia, program coordinator in Kidney Acquisition at MedStar Health

Growing up, I saw firsthand the devastating effects of heart and kidney diseases in my family. My father battled cancer and overcame his illness, but years later, he succumbed to complications after chemotherapy, impacting his cardiac and kidney health. Witnessing his decline deeply affected me and fueled my passion for medicine. Later, my brother was diagnosed with non-Hodgkin lymphoma. Balancing caregiving with my academics and work made me acutely aware of the critical need for accessible and empathetic health care.

As the former KidneyX innovation fellow at the US Department of Health and Human Services, I contributed to pioneering initiatives, including launching the $9.2 million Artificial Kidney Prize Phase 2 and cocreating the KidneyX Sustainability Prize with ASN. My involvement with KidneyX allowed me to witness the transformative power of innovation and reaffirmed my desire to contribute meaningfully to advancing pediatric and adult nephrology. I am inspired by emerging technologies such as bioartificial kidneys and targeted therapies, which will revolutionize treatment.

Currently, I work at MedStar Health as program coordinator in the Kidney Acquisition Department, where I work closely with the kidney and pancreas transplantation teams, dialysis facilities, patients, families, and health care clinicians. Through my journey, I have learned that effective kidney care involves a balance of innovation, compassion, and community engagement. I am committed to advancing this field with my goal of becoming Dr. Araia, a pediatric specialist dedicated to transforming outcomes for children and ensuring that they receive equitable, innovative, and compassionate care throughout their lives.

Natalia Khoshnam, graduate student at Boston University School of Medicine

I did not learn the word "nephrology" from a textbook. I learned it by sitting beside my grandmother in the dialysis clinic. I can still see the faces of the people in the dialysis unit—and feel the quiet ache that settled in when a chair was suddenly empty. My grandmother's name meant butterfly. After she passed, we brought bags of butterfly clips to the unit and handed them out. The small gesture meant something. It said, "She was here. She mattered."

My mother has Alport syndrome. She entered clinical trials and navigated uncertainty, but her kidney function declined. I learned more about nephrology in the quiet aftermath of a phone call when we were told that my mother's kidneys had failed. I grew up translating more than just language. I translated fear and frustration, grief, and uncertainty. Somewhere in the middle of caregiving, advocating, and simply surviving, I realized this was not just my family's story. It was becoming my purpose.

Now, as a graduate student, I study the human systems. But what draws me to nephrology is not only the science. It is the people. It is the interdependence. It is the truth that no one makes it through kidney disease alone. With my mentor, I am conducting research to understand the gaps that prevent patients from connecting to resources, such as the Kidney Support Network. We are aiming to understand where the disconnect begins and how we can help create systems designed for everyone. Nephrology taught me how the body endures. My family taught me how people endure, too. And somewhere between blood pressure cuffs and butterfly clips, I found my calling.

Advice to pre-medical students

Nephrology uniquely connects us with the humanity of our patients, reminding us of the importance of compassion and understanding. In this fast-paced field, it is easy to lose sight of our own humanity and the human element at the core of our work. Many enter nephrology driven by a desire to help others, which also includes supporting the next generation of physicians. Support and empathy are essential to both personal and professional success.

As pre-med students, do not feel ashamed or nervous to speak up about your journey. There are many paths in medicine, and reaching out to potential mentors and professionals can provide valuable guidance. Working closely with nephrologists and kidney advocates has deepened our understanding of the barriers that patients face. Kidney diseases are complex and multifaceted, requiring perspectives from clinical, public health, and patient experiences. Connecting with others in the kidney community not only broadens your understanding but also reinforces the importance of support, empathy, and collaboration in addressing health care challenges. ■

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Resident's Perspective on Pediatric Nephrology: Finding My Vocation

By Ryan C. Ward

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When an immense task is present, the expression, "How do you move a mountain?" is asked, with the answer being "one stone at a time." Pediatric nephrology is currently facing a seemingly mountain-sized task due to the shortage of physicians and unfilled fellowship positions (1, 2). As a resident in the process of applying for a pediatric nephrology fellowship, I venture to offer insight into solutions to the shortage by explaining my path into the field.

I never planned on being a child's kidney doctor, but during medical school, a passionate pediatric nephrologist encouraged me to explore the field. Despite my initial reluctance, I found clinical nephrology far more interesting than expected. I saw cases that one might think only exist in textbooks or lectures, including C3 glomerulonephritis, Fanconi syndrome, and a toddler who was born without functioning kidneys—cases that were unique and complex and beckoned me to delve deeper into pediatric nephrology. Furthermore, every nephrologist who I encountered was great with their patients and wanted students to learn.

Seeking research experience for residency, I contacted that same pediatric nephrologist, who proposed investigating education and employment outcomes in those with pediatric chronic kidney disease. Although it was not what I initially envisioned for my research focus, I pursued it, leading to a sustained interest in neurocognitive outcomes in children with kidney diseases. At the same time, another practitioner candidly discussed with me a career and lifestyle in pediatric nephrology in which no topic was off-limits.

Medical students are advised to choose a specialty for the medicine and patients, not for the specific people with whom they interact. From my experience, however, those people helped shape my interests and exhibited qualities that I wanted to represent. The nephrologists at my home institution are wonderful, and by going to conferences, I discovered that pediatric nephrologists around the globe share the same attitude, generosity, and spirit that I noticed as an M2. As a trainee, if you are looking to work with people who are intelligent and joyful, qualities epitomized in the clinicians with whom I interacted, become a pediatric nephrologist.

For trainees looking for mentorship, I recommend reflecting on what you want your life to look like following training. Even in the busyness of school and residency, the time set apart for self-discovery will be well worth it. Following that self-reflection, identify physicians whose qualities and lifestyle exemplify your ideal future, and ask them to meet and discuss your goals. Then, emulate them. For me, I want to be a nephrologist who is well-versed in the basics of the kidney but is also an encyclopedia within their area of expertise and pushes the field forward through scholarly work. More importantly, I want to be someone who other practitioners, nurses, patients, and families are excited to see and work with—someone who is kind and brings a burst of energy (sometimes in the form of coffee) and joy to the room. Is there a greater compliment than when families ask: "Is Dr. So-and-So going to come by?" These are the traits that I find in my mentor and are goals to achieve for my own career.

"But the kidney is complicated!" is an often-heard refrain. It is true that the physiology can be challenging. However, the kidney is also awe-inspiring. It is integral to electrolytes, fluid balance, and acid-base status and is tightly linked to cardiovascular function, blood cell production, bone health, genetics, cognition, growth, quality of life, and rheumatology. Hypertension management touches on general pediatrics, and immunology and infectious diseases come into play in transplant. This knowledge is not limited to the clinic, either. The intensive care unit often calls the nephrologist for aid with filtration and clearance. Nephrologists have to be a jack-of-all-medical-specialties and an ace in the kidney. I argue that this is how nephrology should be presented to trainees.

I do not have a sophisticated, five-point plan for addressing the pediatric nephrology physician shortage. But I believe that if we focus on what makes the kidney spectacular and the people who make it a special field, then we will attract special people. As in my case, there is power in attendings and mentors who are willing to invest time and effort into a learner—one medical student, one resident at a time. ■

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Detective Nephron

Detective Nephron, world-renowned for his expert analytic skills, trains budding physician-detectives in the diagnosis and treatment of kidney diseases. Mackenzie Ula Densa (Mac), a budding nephrologist, plans to present a new case to the master consultant.

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Charts, lab slips, and a cup of black coffee lie in front of Detective Nephron. Mac enters with nervous excitement, holding a thick folder.

Mac Detective, I've brought you a puzzling case.

Nephron (*sipping coffee*) Ah, my favorite. Let's see if this mystery is worthy of our time.

Mac (*flipping through the chart*) A 74-year-old woman, no significant alcohol use or surgery, presents with persistent nausea, vomiting, tremors of the hands, and confusion. Her family describes her as "not herself" for several days.

Nephron Confusion in the older adult…many suspects: infection, stroke, medications, metabolic disturbances. What do the labs say?

Mac That's where it gets interesting. She had severe hypomagnesemia at 0.7 mg/dL on admission. Also, low calcium at 1.62 mmol/L and low potassium.

Nephron (*leaning in*) A trio of abnormalities: hypomagnesemia, hypokalemia, and hypocalcemia. Tell me about the parathyroid hormone (PTH).

Mac (*smirking*) I knew you were a budding endocrinologist. Normal PTH. Right in the reference range.

Nephron (*raising a brow*) Normal PTH in the setting of hypocalcemia? That's physiologically inappropriate. Either the parathyroids are stunned, or something is suppressing their release. Magnesium often holds the key.

Mac Exactly! But the renal evaluation shows that her kidneys are trying to conserve magnesium—low fractional excretion.

Nephron So not renal wasting.

Nephron tickles his fingers as he paces.

Mac When I think of hypomagnesemia, I think decreased intake: malnutrition or alcoholism; gastrointestinal losses: chronic diarrhea, malabsorption syndromes, or small bowel resections; renal wasting: loop or thiazide diuretics, aminoglycosides, cisplatin, calcineurin inhibitors, or inherited tubulopathies; endocrine causes: hyperaldosteronism or hyperthyroidism; and, finally, medications impairing absorption: most notably, proton pump inhibitors (PPIs).

Nephron (*turning to Mac*) Now, which suspect fits best here?

Mac She's well nourished, no diarrhea, no diuretics or chemo, no endocrine disorder, but she has been on omeprazole daily for nearly 10 years.

Nephron That leaves reduced gastrointestinal absorption. Did she have malabsorption syndrome?

Mac Not to my knowledge.

Nephron (*snapping fingers*) Well, then the PPI is the thief! It's robbing her of magnesium slowly but relentlessly.

(*leaning back, smiling knowingly*) Ah, the PPI…an old friend in these mysteries. Tell me, Mac, what do PPIs do to magnesium absorption?

Mac (*thinking*) They block the transient receptor potential melastatin types 6 and 7 (TRPM6 and TRPM7) magnesium channels in the gut, impairing active magnesium absorption. Over years, it can lead to profound hypomagnesemia.

Nephron Precisely. The clinical fingerprints are clear: chronic PPI use, magnesium loss not explained by the kidney, and a cascade of secondary issues. Without magnesium, the parathyroids cannot secrete PTH effectively, leading to functional hypoparathyroidism. And without PTH, calcium drops. Meanwhile, hypomagnesemia enhances renal potassium wasting, hence the low potassium.

Mac That explains the delirium, tremors, and even her horizontal nystagmus. Omeprazole was the culprit here. But, do *all* PPIs cause hypomagnesemia?

Nephron (*smiling, as if expecting the question*) Excellent, Mac. The answer is yes. Hypomagnesemia has been reported with *all* PPIs: omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole. It's considered a class effect.

Mac Is it dose related? Or only after many years?

Nephron (*bored*) Another sharp question. It usually occurs after long-term therapy—often more than 1 year, sometimes even 1 decade, as in our patient. But cases have been described within months. The risk is not clearly dose-dependent. Instead, it's related to how PPIs impair TRPM6/7 magnesium transport channels in the gut, limiting absorption regardless of serum demand.

Mac So switching from one PPI to another won't fix the problem?

Nephron Exactly. If hypomagnesemia develops on one PPI, it will likely recur with another. The only true solution is stopping the entire class. If acid suppression is still needed, H_2 receptor blockers (like famotidine) can be used instead. Remember, Mac, the PPI may look innocent on the medications list, but it's a repeat offender in the case files of hypomagnesemia.

Mac Detective, if all PPIs are guilty, what about the newer acid reflux drugs? Could they be safer?

Nephron (*smiling knowingly*) You must be referring to the potassium-competitive acid blockers, or P-CABs, like vonoprazan.

Mac Yes, that's the one. Do they also cause hypomagnesemia?

Nephron Excellent question. P-CABs work differently: Instead of irreversibly blocking the proton pump like PPIs, they competitively and reversibly block the potassium-binding site on the gastric H^+/K^+-ATPase. Because of this, they achieve faster, more potent acid suppression than PPIs. I think they can cause acute interstitial nephritis similar to PPIs.

Mac And the magnesium?

Nephron To date, clinically significant hypomagnesemia hasn't been reported with vonoprazan or other P-CABs. Their mechanisms do not appear to impair intestinal TRPM6/7 magnesium transport the way that PPIs do. However, these drugs are relatively new. Long-term safety data are still limited. We must remain cautious before declaring them completely innocent.

The jury is still out. But for patients with severe PPI-induced hypomagnesemia who still require acid suppression, P-CABs may one day offer a safer alternative. Until then, the safest strategy is to stop the offending agent, switch to an H_2 blocker, and monitor electrolytes closely.

A few moments of silence

Nephron A perfect storm of electrolyte chaos. What happened when you stopped the culprit?

Mac Omeprazole was discontinued. She was given magnesium, calcium, and potassium supplementation. Within 3 days, her calcium normalized, and supplementation could be tapered. By 1 week, her PTH rebounded, and her neurological symptoms resolved.

Nephron Elegant. Remove the trigger, restore the balance.

Mac I realized that I have to always think *magnesium* when I see unexplained hypocalcemia or refractory hypokalemia. Normal PTH with low calcium is a red flag for hypomagnesemia suppressing secretion. PPIs—widely used, often forgotten—are a common and reversible culprit.

(*smiling*) Another mystery solved, detective.

Nephron (*standing up, grabbing his NY-style coffee*) Indeed, Mac. But beware! The most dangerous villains are often the ones hiding in plain sight, prescribed every day without suspicion. ■

Detective Nephron was developed by Kenar D. Jhaveri, MD, FASN, professor of medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY. Special thanks are given to Rimda Wanchoo, MD, professor of medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell; Sam Kant, MD, FASN, attending nephrologist and transplant physician at St. Vincent's University Hospital, University College Dublin, Ireland; and Prakash Gudsoorkar, MD, FASN, assistant professor of medicine at the University of Cincinnati, OH, for their editorial assistance. Send correspondence regarding this column to kjhaveri@kidneynews.org.

Renal Tubular Alkalosis: A Novel Renal Syndrome?

By Nabil William G. Sweis and Daniel Batlle

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Renal tubular acidosis (RTA), described nearly 1 century ago, has long been a preferred topic of discussion for students of kidney diseases (1). The primary forms of distal RTA (dRTA), in particular, provide insights on how malfunction of transport proteins in the α-intercalated cells in the distal nephron results in failure to excrete acid and, consequently, the development of metabolic acidosis (2, 3). A recent study by Peng et al. (4) describes—to our knowledge, for the first time—what can be viewed as the alkalotic counterpart of primary dRTA and thus be termed distal renal tubular alkalosis.

Among the several transporters involved in the regulation of acid excretion by α-intercalated cells is a vacuolar H^+-ATPase that pumps protons against a pH gradient from the apical side in the collecting tubule to the tubular urine (2). Because of the activity of this pump in α-intercalated cells, acting in concert with other acid-base transporters, hydrogen ions are secreted and bind to urinary buffers like ammonia and phosphate. As such, the elimination of secreted hydrogen ions combined with these urinary buffers provides an effective way to fine-tune the excretion of the dietary acid load. In dRTA, however, the urine pH cannot be maximally lowered, and acid excretion in the form of ammonium cannot sustain the need for acid excretion imposed by the acid load generated by most Western diets (2, 3). As a result, metabolic acidosis ensues, and when the disease manifests itself early in life, there are devastating consequences for bone health, with delayed growth, and deposition of calcium in the kidneys in the form of nephrocalcinosis and recurring kidney stones (2, 3).

To make matters worse, the excretion of potassium in the urine is increased, and severe hypokalemia can develop, leading to muscle weakness and, occasionally, paralysis (2, 3). Mutations in genes encoding subunits of the vacuolar H^+-ATPase, including *ATP6V0A4* and *ATP6V1B1*, which encode the a4 and B1 subunits, respectively, can cause autosomal recessive dRTA (5). Such mutations result in alterations in pump assembly or trafficking to the apical membrane, such that the ability to secrete hydrogen ions is greatly reduced (3, 5, 6).

What if instead of a loss-of-function mutation, patients would present with clinical manifestations attributable to a gain-of-function mutation in the *ATP6V0A4* or *ATP6V1B1* genes? The clinical picture should be enhanced—rather than decreased—hydrogen ion secretion, with the development of metabolic alkalosis rather than metabolic acidosis.

One such mutation has been described, to our knowledge, for the first time in a 32-year-old male patient and his father with a heterozygous gain-of-function mutation in the *ATP6V0A4* gene, which encodes the a4 subunit of vacuolar H^+-ATPase (4). Both the father and the son had metabolic alkalosis, and, interestingly, both also had hypokalemia. Such a gain-of-function mutation and the associated clinical phenotype have not been previously described, suggesting a new renal syndrome that is the mirror image of dRTA (7).

The renal and extrarenal manifestations, however, are only partially the opposite of dRTA (Figure). In fact, some manifestations, like hearing impairment and hypokalemia, are common to both (7). Also, a mirror image of hypokalemic dRTA would be hyperkalemic distal renal tubular alkalosis. However, in both the son and the father with the described novel gain-of-function mutation in *ATP6V0A4*, striking hypokalemia and hearing impairment were reported (4). These two manifestations are also often seen with loss-of-function mutations of the a4 and B1 subunits of vacuolar H^+-ATPase (3, 5, 6). It is very important to keep an optimal pH in the endolymphatic fluid for hearing acuity, and a disruption of the fluid pH there by under- or overactivity of the a4 subunit of vacuolar H^+-ATPase may result in sensorineural hearing loss.

How would such a metabolic alkalosis caused by a gain-of-function mutation of *ATP6V0A4* be treated? This is clearly a new challenge. Would acid rather than alkali be provided as the medical therapy? The consequences of long-term acid administration for a chronic disease in the form of HCl, to our knowledge, are totally unknown. Fostering the excretion of bicarbonate with salt tablets could actually be counterproductive, as it would favor sodium-dependent hydrogen ion secretion via the mutated overactive vacuolar H^+-ATPase. Perhaps the administration of a carbonic anhydrase inhibitor should help correct the metabolic alkalosis. Finally, such a mutation should be a prime target for gene therapy. This is in contrast to dRTA, with which alkali therapy can take care of most manifestations except for hearing impairment (8). Unfortunately, the patient in the study by Peng et al. (4) was evaluated later in life, and, compounding the situation, he had already developed advanced chronic kidney disease (CKD).

Although the primary or hereditary forms of dRTA are relatively rare, they have captured the imagination and interest of nephrology as a specialty (1). This newly described syndrome of renal tubular alkalosis should keep us alert for new cases of a very likely, ultrarare but fascinating disease that can teach us about physiology and biology of the kidney and would challenge us on how to treat metabolic alkalosis on a long-term basis. Another final thought is whether a gain-of-function mutation in *ATP6V0A4* could have an impact on progression of CKD. It would be of interest to examine whether in the current search for unknown genes involved in unexplained CKD, *ATP6V0A4* mutations can be found. ■

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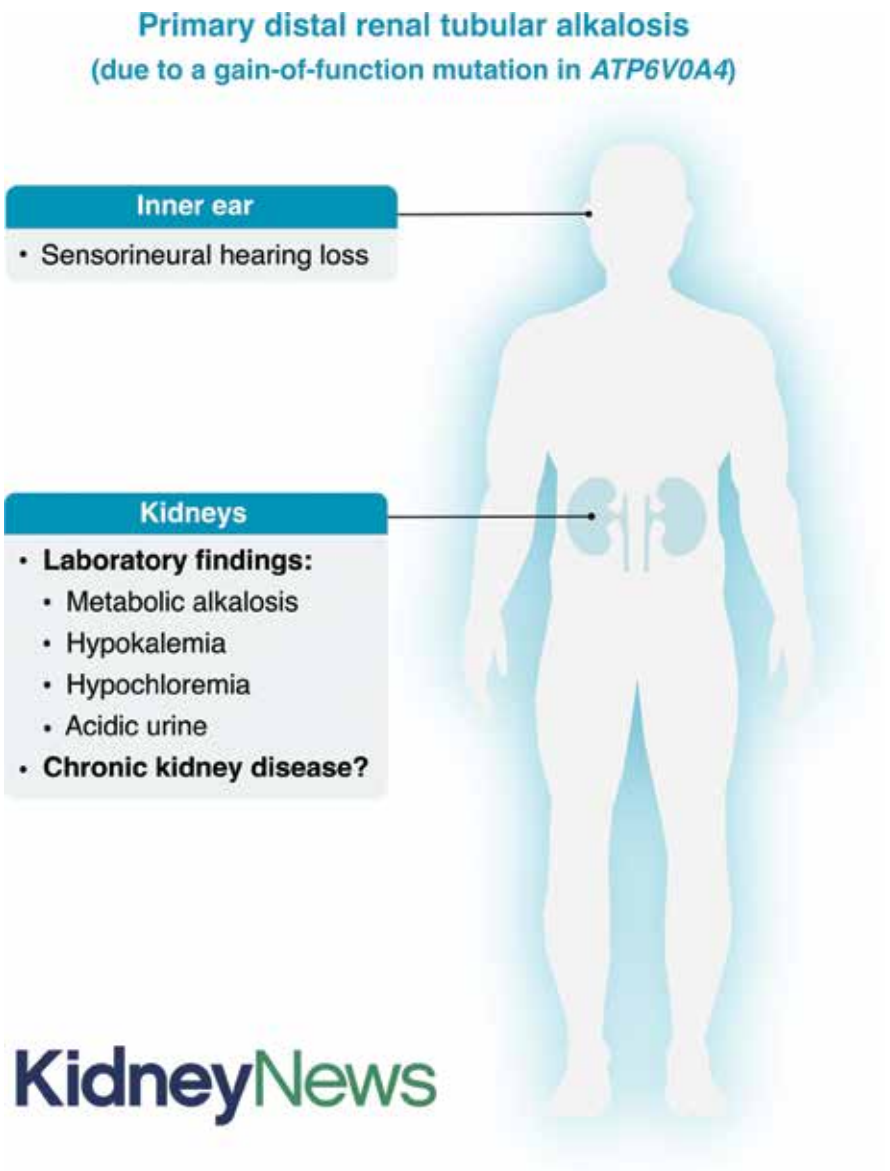
The authors report no conflicts of interest.

Figure. Clinical features of the reported syndrome of distal renal tubular alkalosis



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HighVolumeHDF: The Next Standard of Care for US Patients - Evidence and Practical Use

Presented by FRESENIUS MEDICAL CARE

11:00–11:45 a.m. — **Theater 2**

Global Pathways to Home: Strategies for Success

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11:30 a.m.–12:15 p.m. — **Theater 3**

Expert Perspectives and Patient Experiences: Upgrading to a Stronger Foundation in IgA Nephropathy

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12:00–12:45 p.m. — **Theater 1**

Advancing Care in Lupus Nephritis: Exploring the Evolving Landscape

Presented by Genentech, A Member of the Roche Group

12:30–1:15 p.m. — **Theater 2**

Houston, We Have a Solution: Integrating Genetics into Clinical Practice

Presented by natera

1:00–1:45 p.m. — **Theater 3**

B-cell Modulation in IgA Nephrology and a Patient Case Study

Presented by Otsuka

Friday, November 7

10:00–10:45 a.m. — **Theater 1**

Decoding a Silent Threat: Aldosterone's Impact on Hypertension and Cardiovascular and Renal Morbidity

Presented by AstraZeneca

11:00-11:45 a.m. — **Theater 2**

Expanding Perspectives in Hyperphosphatemia Treatment; A Different Approach

Presented by ardelyx

11:30 a.m.–12:15 p.m. — **Theater 3**

IgA Nephropathy Paradigm Shift: KDIGO Guidelines and the Centrality of B Cells

Presented by VERTEX

Friday, November 7 (Continued)

12:00–12:45 p.m. — **Theater 1**

Hypoxia-Inducible Factor Activation & Erythropoietic Effects in Anemia due to CKD

Presented by Akebia THERAPEUTICS

12:30–1:15 p.m. — **Theater 2**

Navigating the Crossroads of IgAN: 2 Distinct Paths to Reducing Proteinuria

Presented by NOVARTIS

1:00–1:45 p.m. — **Theater 3**

Targeting IgAN Early: Considerations for Adding Potentially Disease Modifying Therapy to Frontline Treatment

Presented by calliditas THERAPEUTICS

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Jardiance® (empagliflozin) tablets: Expert Perspectives on Clinical Trial Data and Approved Indications

Presented by Boehringer Ingelheim | Lilly

11:30 a.m.–12:15 p.m. — **Theater 3**

Taking a Different Direction in the Treatment of Primary Hyperoxaluria Type 1 (PH1)

Presented by novo nordisk®

12:00-12:45 p.m. — **Theater 1**

Role of CD38+ Cells in Immune-Mediated Kidney Disease

Presented by Biogen

12:30–1:15 p.m. — **Theater 2**

Translating KDIGO Guidelines into Therapeutic Goals in IgA Nephropathy

Presented by vera therapeutics

1:00–1:45 p.m. — **Theater 3**

DefenCath® Indication, Use and Navigating Reimbursement Across Settings of Care

Presented by CorMedix

Educational Symposia Schedule

KIDNEY WEEK 2025

Hilton Americas-Houston (Level 4)
Thursday, November 6–Saturday, November 8
12:45–1:45 p.m. Daily

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
These live activities are eligible for continuing education credit.
Please visit www.asn-online.org/KidneyWeek for more information.

Thursday, November 6

Breaking Barriers: Advances in Understanding and Treating Complement-Mediated Kidney Diseases
*Support is provided by an educational grant from **Novartis Pharmaceuticals Corporation.***

Hypoxia-Inducible Factor-Prolyl Hydroxylase Inhibitors, CVD, and Hyporesponsiveness to Erythropoiesis-Stimulating Agents in ESKD
*Support is provided by an educational grant from **Akebia Therapeutics, Inc**.*

Prevention of CKD-Associated Hyperphosphatemia in 2025: What Are the Risks and Benefits?
*Support is provided by an educational grant from **Ardelyx, Inc**.*

Role of Complement in ANCA-Associated Vasculitis
*This activity is supported by educational funding provided by **Amgen**.*

Friday, November 7

Considerations for Incorporating Hemodiafiltration into Dialysis Care
*Support is provided by an educational grant from **Fresenius Medical Care.***

Expanding Therapeutic Horizons in IgAN
*Support is provided by educational grants from **Otsuka America Pharmaceutical, Inc. and Vera Therapeutics, Inc.***

Inflammation at the Crossroads: Atherosclerotic Cardiovascular Disease and CKD Interactions
*Support is provided by an educational grant from **Novo Nordisk.***

Optimizing B Cell-Targeted Therapies for Lupus Nephritis: Strategies for Success and Pitfalls to Avoid
*Support is provided by an educational grant from **Genentech, a member of the Roche Group.***

Saturday, November 8

AKI and Hepatorenal Syndrome: Diagnosis, Management, and Treatment
*Support is provided by an educational grant from **Mallinckrodt Pharmaceuticals.***

Management of RAAS Inhibitor Therapy After Hyperkalemia in Patients with CKD and Heart Failure
*Support is provided by an educational grant from **AstraZeneca.***

Proteinuria and eGFR as Clinical Trial End Points in FSGS
*Support is provided by an educational grant from **Travere Therapeutics, Inc.***

All symposia will be recorded and available in the ASN eLearning Center for up to three years starting in late November; continuing education credits will not be awarded for the online content.

PLENARY SESSION

STATE-OF-THE-ART LECTURE

Global Trials Leader to Deliver State-of-the-Art Lecture on the Future of Curing Kidney Diseases

https://doi.org/10.62716/kn.001872025

Vlado Perkovic, MBBS, PhD, FASN

A leader in global clinical trials and kidney therapeutics will deliver the state-of-the-art lecture on Thursday, November 6, during the opening plenary session. Vlado Perkovic, MBBS, PhD, FASN, will present "Yes We Can…Cure Kidney Diseases," followed by an expert panel.

Dr. Perkovic is provost and scientia professor at the University of New South Wales (UNSW) Sydney in Australia. A globally recognized nephrologist and clinical investigator, he has led and contributed to many of the most influential clinical trials in kidney diseases over the past 2 decades—work that has redefined standards of care and supported the approval of new therapies.

Dr. Perkovic previously served as dean of the Faculty of Medicine and Health at UNSW Sydney and as executive director of The George Institute for Global Health, where he played a key role in building George Clinical (now Emerald Clinical Trials), an international contract research organization founded by the institute and now operating as an independent company. He continues to serve on the boards of George Clinical, St Vincent's Health Australia, and several other major medical research institutions.

Dr. Perkovic's research has focused on improving outcomes for people with kidney diseases through rigorous, high-impact international trials. He has led the steering committees for landmark studies that directly informed the approval of three first-in-class therapies for kidney diseases. Most recently, he helped establish the first global patient registry and platform trial for chronic kidney disease, a major initiative to accelerate innovation and expand trial access worldwide.

In addition to his research, Dr. Perkovic has contributed to clinical care standards through his leadership in guideline development for kidney diseases, blood pressure management, and cardiovascular risk. He is a past chair of the International Society of Nephrology's Advancing Clinical Trials initiative and the Scientific Committee of the Australasian Kidney Trials Network. He has also served as president of the Association of Australian Medical Research Institutes and on the board of the Australian Clinical Trials Alliance from 2016 to 2018.

Dr. Perkovic has coauthored more than 400 peer-reviewed publications and 13 book chapters. His work is widely cited, and he is considered a thoughtful leader on trial methodology, regulatory strategy, and accelerating innovation in the treatment of kidney diseases.

He received his medical degree from The Royal Melbourne Hospital and earned a PhD from The University of Melbourne. He is a fellow of the Royal Australasian College of Physicians, the Australian Academy of Health and Medical Sciences, and ASN.

Clinical trials expert panelists:

Julie R. Ingelfinger, MD
Harvard Medical School and Massachusetts General Hospital, Boston, MA

Alan S. Kliger, MD
Yale University School of Medicine, New Haven, CT

Patient Advocacy Leader to Speak on the Power of Partnership in IgA Nephropathy Research

https://doi.org/10.62716/kn.001512025

Bonnie Schneider

A pioneering patient advocate and nonprofit leader will deliver the Celeste Castillo Lee Endowed Lectureship on Thursday, November 6, during the session "Success Stories in Glomerular Diseases: From Bench to Bedside." Bonnie Schneider, cofounder and director of the IgA Nephropathy Foundation, will present a lecture titled "Importance of Patient Advocate Partners to Get Discoveries to the Bedside."

Ms. Schneider is a nationally recognized voice for patients affected by immunoglobulin A nephropathy (IgAN). Her journey began in 2004, when her then 13-year-old son Eddie was diagnosed with the disease. At that time, there were few resources for patients, little public awareness, and virtually no ongoing research. The experience of navigating this unfamiliar diagnosis alone prompted Ms. Schneider and her husband, Ed, to take action. She left her marketing career in New York City and cofounded the IgA Nephropathy Foundation, with a mission to ensure that no other family would have to face IgAN in isolation.

Under her leadership, the foundation has grown into one of the only patient-centered organizations in the United States dedicated solely to IgAN. It has become a powerful hub for community support, education, and advocacy and a driver of research progress. By mobilizing patients in the IgAN community, the foundation has helped shape clinical trial priorities, connected patients with researchers, and raised awareness of the disease on national and international levels.

Ms. Schneider has been instrumental in building partnerships across the nephrology landscape, serving as a collaborator to academic researchers, pharmaceutical sponsors, and policy groups. In 2025, she was honored as the first keynote speaker at the 18th International Symposium on IgA Nephropathy, a milestone that acknowledged the central role of patient voices in advancing glomerular disease research.

As a full-time director of the foundation, Ms. Schneider continues to champion efforts that bring patients into the center of discovery and care delivery. The foundation's guiding philosophy—"by patients, for patients"—reflects her belief that meaningful progress in rare diseases depends on partnerships among advocates, clinicians, and scientists.

Ms. Schneider lives in Wall, NJ, with her husband and enjoys spending time with their five children and two grandchildren. She is grateful for the community that has grown around the foundation and proud to know that today, no one has to face an IgAN diagnosis alone.

Glomerular Diseases and Pregnancy to Be Subject of Winn Lectureship

https://doi.org/10.62716/kn.001652025

Michelle A. Hladunewich, MD, MS, FASN

A clinical leader in glomerular diseases will deliver the Michelle P. Winn, MD, Endowed Lectureship on Thursday, November 6. Michelle A. Hladunewich, MD, MS, FASN, will speak on "Diagnosis and Management of Pregnancy Complications in Glomerular Diseases."

Dr. Hladunewich serves as physician-in-chief in the Department of Medicine at Sunnybrook Health Sciences Centre in Toronto, Ontario, Canada, where she is also a staff member in the Divisions of Nephrology and Obstetrical Medicine. Furthermore, she is an associate scientist in biological sciences for the DAN [Diversity, Access, and Needs] Women & Babies Research Program at Sunnybrook Research Institute.

In addition, she is a professor in the Division of Nephrology at the University of Toronto's Department of Medicine. She serves as the provincial medical lead for glomerulonephritis and specialty clinics, including pregnancy, for the Ontario Renal Network.

Dr. Hladunewich studies glomerular diseases and pregnancy-related kidney diseases. At Sunnybrook Health Sciences Centre, she leads the Pregnancy and Kidney Disease (PreKID) Clinic, where she cares for pregnant individuals with kidney diseases before, during, and after pregnancy and collects data to improve future care. As a co-principal investigator of the Cure Glomerulonephropathy (CureGN) consortium, she is part of an international team, working to understand and address glomerular diseases in both adults and children. Her other research interests include acute kidney injury, as well as the effects of preeclampsia, hormone therapy, and other clinical scenarios on the kidneys.

In recognition of her contributions, Dr. Hladunewich has been named an ASN fellow and an elected member of the American Physiological Society. In 2021, she received the ASN Distinguished Clinical Service Award for midcareer professionals. She has also earned numerous research awards, including an Innovation in Laboratory Medicine Award from the Canadian Society of Clinical Chemists for her work on preeclampsia biomarkers.

Dr. Hladunewich received her MD from the University of Alberta. She completed a residency in general internal medicine at the University of Toronto's Department of Medicine and served as chief medical resident in the Department of Medicine, Sunnybrook Health Sciences Centre. She then completed fellowships in critical care medicine and nephrology and earned a master's degree in epidemiology and clinical research at Stanford Medicine.

Diabetes Researcher to Provide Update on SGLT2 Inhibitors

https://doi.org/10.62716/kn.001712025

Ralph A. DeFronzo, MD

An eminent type 2 diabetes researcher will deliver the Barry M. Brenner, MD, Endowed Lectureship on Thursday, November 6. Ralph A. DeFronzo, MD, will present a lecture titled "SGLT2 Inhibitor Journey: From Metabolism to Kidney and Heart Protection."

Dr. DeFronzo is a professor of medicine and chief of the Division of Diabetes at The University of Texas Health Science Center at San Antonio (UT Health San Antonio) Long School of Medicine and deputy director of the Texas Diabetes Institute at University Health. He also holds the Joe R. & Teresa Lozano Long Distinguished Chair in Diabetes at the Long School of Medicine at UT Health San Antonio.

His research focuses on the development, progression, and treatment of type 2 diabetes, including the central role of insulin resistance. In 1995, he helped gain US Food and Drug Administration (FDA) approval for metformin, now used as the first-line medication treatment for type 2 diabetes. He was instrumental in establishing the use of sodium-glucose cotransporter-2 (SGLT2) inhibitor drugs in type 2 diabetes by showing their effect on renal glucose reabsorption, leading to the FDA approval of dapagliflozin, empagliflozin, and canagliflozin.

In 2028, Dr. DeFronzo will have received funding from the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health (NIH), for 53 consecutive years (beginning in 1975). He currently serves as principal investigator or coinvestigator on four NIH grants focused on type 2 diabetes. He has published more than 850 peer-reviewed articles and edits the *International Textbook of Diabetes Mellitus*.

In recognition of his work, Dr. DeFronzo has received numerous national and international awards, including the Banting Medal for Scientific Achievement, the highest scientific award conferred by the American Diabetes Association (ADA), and the Claude Bernard Prize from the European Association for the Study of Diabetes. He won the Harold Hamm International Prize for Biomedical Research in Diabetes from The University of Oklahoma in 2017 and the Prince Mahidol Award, which honors major contributions to global health care, from its foundation in 2022. He also received the Albert Renold Award from ADA to honor his mentorship and training of more than 200 young diabetes investigators.

Dr. DeFronzo received his medical degree from Harvard Medical School before completing a residency in internal medicine at The Johns Hopkins Hospital and a fellowship in endocrinology at Johns Hopkins Bayview Medical Center, both administered by the Johns Hopkins School of Medicine, Baltimore, MD. He also completed a fellowship in nephrology at the Hospital of the University of Pennsylvania, administered through the Perelman School of Medicine, Philadelphia, PA.

Inaugural Silbiger Lecture to Cover Hypertension and Pregnancy

https://doi.org/10.62716/kn.001862025

Vesna D. Garovic, MD, PhD, FASN

A renowned hypertension and nephrology researcher will deliver the inaugural Sharon Silbiger, MD, Endowed Lectureship on Thursday, November 6. Vesna D. Garovic, MD, PhD, FASN, will present a talk titled "Hypertension and Pregnancy."

The new lectureship honors the life and legacy of Sharon R. Silbiger, MD, a noted nephrologist who made key research contributions on the role of biological sex in chronic kidney disease progression. The lectureship was established by ASN and Women in Nephrology, of which Dr. Silbiger served as president in 2009–2010.

Dr. Garovic is professor of medicine at the Mayo Clinic, Rochester, MN, with primary appointments in the Division of Nephrology and Hypertension and the Department of Internal Medicine and a joint appointment in the Department of Obstetrics and Gynecology. She is also dean for Clinical and Translational Science, director of the Center for Clinical and Translational Science, chair of the Division of Nephrology and Hypertension, and associate chair for research in the Department of Medicine. She received the Penske Foundation Professorship in Clinical Medicine in Honor of Ian D. Hay, MD, PhD, and J. Eileen Hay, MBChB, which is one of the highest academic distinctions at the Mayo Clinic.

Dr. Garovic's research centers on hypertension and nephrology, with a particular focus on women's health. She studies hypertensive disorders of pregnancy, focusing on preeclampsia and the mechanisms that underlie kidney damage and proteinuria. She also studies the role of epigenetics in preeclampsia and how the condition alters future risk for cardiovascular and kidney diseases. Her research has resulted in more than 200 peer-reviewed publications.

Several awards have honored Dr. Garovic's contributions. In 2024, she received ASN's Barbara T. Murphy lifetime achievement award. She has also acquired both the Arthur C. Corcoran Memorial Lecture award and the Marvin Moser Clinical Hypertension Award from the American Heart Association Council on Hypertension. She is a fellow of both the American Heart Association and ASN.

She received her medical degree and a master's degree in biochemistry and accomplished her medical residency training in obstetrics and gynecology at the University of Belgrade Faculty of Medicine in Serbia. She also completed a residency in internal medicine and a fellowship in nephrology at the Montefiore Medical Center through the Albert Einstein College of Medicine. In addition, Dr. Garovic has earned a master's degree in medical genetics from McGill University in Montreal, Quebec, Canada, and a PhD from the Department of Obstetrics and Gynecology at the University of Belgrade Faculty of Medicine with a focus on molecular biology.

PLENARY SESSION

STATE-OF-THE-ART LECTURE

Plenary to Focus on Systems Biology of Kidney Diseases

https://doi.org/10.62716/kn.001582025

Julio Saez-Rodriguez, PhD

A leading bioinformatics researcher will deliver a state-of-the-art lecture on "Systems Biology of Kidney Diseases" at a plenary session on Friday, November 7, followed by an expert panel.

Julio Saez-Rodriguez, PhD, is head of research at the European Bioinformatics Institute, which supports research in the life sciences by managing large-scale biological datasets and related tools. The European Bioinformatics Institute is located on the Wellcome Genome Campus in Hinxton, England, and is part of the European Molecular Biology Laboratory, an organization that unites independent research groups across Europe.

Dr. Saez-Rodriguez is also a professor (on leave) of medical bioinformatics and data analysis and director of the Institute for Computational Biomedicine at Heidelberg University in Germany. He is a member of the Heidelberg unit of the European Laboratory for Learning and Intelligent Systems, an artificial intelligence research network, and is a codirector of Dialogue on Reverse Engineering Assessment and Methods (DREAM) challenges, which promotes open and collaborative science to tackle unanswered questions in biology and medicine.

Through his research, Dr. Saez-Rodriguez aims to develop new therapies for a range of diseases, including cancer and autoimmune and cardiovascular diseases, based on an understanding of how biological signaling becomes deregulated. He uses several approaches in his work, including large-scale "omics" studies and models of various biological subsystems. He has a particular interest in leveraging existing biological knowledge to inform and enhance computational analysis.

Dr. Saez-Rodriguez applies his computational modeling expertise to kidney diseases by integrating diverse molecular datasets—such as time-resolved, single-cell, and spatial omics—with causal network approaches to better understand disease progression. He has contributed to large-scale efforts to map the kidney tissue proteome and has helped define how these molecular insights can guide biomarker discovery and therapeutic development.

Dr. Saez-Rodriguez received his PhD in chemical engineering from Otto von Guericke University Magdeburg in Germany. He completed postdoctoral training in biological engineering at Harvard Medical School and Massachusetts Institute of Technology. Before joining the faculty at Heidelberg University, he was a professor of computational biomedicine at Rheinisch-Westfälische Technische Hochschule Aachen in Germany, commonly known as RWTH Aachen University.

Expert panelists:

Laura Barisoni, MD
Duke University, Durham, NC

Matthias Kretzler, MD
University of Michigan, Ann Arbor, MI

Navdeep Tangri, MD, PhD
University of Manitoba, Winnipeg, Canada

John P. Peters Award to Honor Harold I. Feldman for Decades of Research Into Renal Insufficiency

https://doi.org/10.62716/kn.001542025

Harold I. Feldman, MD, MS, MSc, FASN

ASN will recognize the wide-ranging contributions of Harold (Harv) I. Feldman, MD, MS, MSc, FASN, with the presentation of the John P. Peters Award on Friday, November 7. This award is given for outstanding contributions to improving the lives of patients and furthering the understanding of the kidney in health and disease.

Dr. Feldman is deputy executive director for Patient-Centered Research Programs at the Patient-Centered Outcomes Research Institute and editor-in-chief of the *American Journal of Kidney Diseases*. He is also professor emeritus of medicine and epidemiology at the Perelman School of Medicine at the University of Pennsylvania.

Dr. Feldman is internationally recognized for his contributions to nephrology research. He led the Chronic Renal Insufficiency Cohort Study, a large-scale observational study of chronic kidney disease funded by the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, for more than 20 years. The Chronic Renal Insufficiency Cohort Study produced a number of highly impactful findings, including the progression and comorbidity burden of chronic kidney disease, as well as its impact on quality of life. To broaden the study's research, Dr. Feldman also established the Chronic Renal Insufficiency Ancillary Studies, resulting in more than 140 independently funded studies, and the International Network of Chronic Kidney Disease, a global network of chronic kidney disease cohorts. He has published more than 350 peer-reviewed articles on topics related to kidney health and disease.

During his tenure at the Perelman School of Medicine, Dr. Feldman chaired the Department of Biostatistics, Epidemiology, and Informatics, the university's largest basic science department. He also led the Robert Wood Johnson Foundation Clinical Scholars Program and the Master of Science in Clinical Epidemiology program. He is past president of the American College of Epidemiology and has served as scientific adviser for multiple institutions, including the National Kidney Foundation, the Scientific Registry of Transplant Recipients, and the US Renal Data System.

Dr. Feldman has received numerous awards and honors from the University of Pennsylvania, including the Arthur K. Asbury Outstanding Faculty Mentor Award. He is a member of the Association of American Physicians, the American Epidemiological Society, and The American Society for Clinical Investigation. He is a fellow of the American College of Physicians and ASN.

He received his medical degree from Boston University School of Medicine, now Boston University Chobanian and Avedisian School of Medicine. He then completed a residency in internal medicine at the University of California, Los Angeles. After residency, he joined the Perelman School of Medicine, where he completed an Andrew W. Mellon Foundation fellowship in clinical epidemiology and general medicine, a fellowship in the Division of Renal Electrolyte and Hypertension in the Department of Medicine, and a master's degree in clinical epidemiology. He completed the Chief Learning Officer program at the University of Pennsylvania Graduate School of Education. He studied advanced biostatistics and epidemiology at the New England Epidemiology Institute at Tufts University.

Pioneering Researcher Katalin Susztak to Receive Homer W. Smith Award

https://doi.org/10.62716/kn.001592025

Katalin Susztak, MD, PhD

Prominent physician-scientist Katalin Susztak, MD, PhD, will be presented the Homer W. Smith Award on Friday, November 7. This award recognizes outstanding contributions to understanding how kidneys function in normal and diseased states.

Dr. Susztak is professor of medicine and nephrology at the Perelman School of Medicine at the University of Pennsylvania, Philadelphia. She holds secondary appointments in the Department of Genetics at the Perelman School of Medicine and in the Department of Pediatrics at Children's Hospital of Philadelphia (CHOP). She directs the University of Pennsylvania Diabetic Nephropathy Program and codirects the Penn-CHOP Kidney Innovation Center. Previously, she was associate professor of medicine and genetics at the Albert Einstein College of Medicine.

She and her research group have made critical contributions toward understanding the genetic and molecular mechanisms that underlie chronic kidney disease (CKD). After developing a large human kidney tissue bank, she identified several novel risk genes for CKD, including *DAB2*, *DPEP1*, *LACTB*, and *MANBA*, highlighting the importance of proximal tubules in regulating kidney function. Her large-scale epigenomic studies have shown the key role of cytosine methylation and other epigenetic changes in CKD. In addition, Dr. Susztak's laboratory was the first to create a single-cell RNA sequencing atlas of the mammalian kidney, revealing the role of certain cell types in CKD. She also launched the Transformative Research in Diabetic Nephropathy consortium, a public–private partnership to understand and treat diabetic kidney disease.

Dr. Susztak has published more than 250 peer-reviewed papers in high-impact journals. She is on the editorial boards of several journals, including *JASN*, *The Journal of Clinical Investigation*, *Kidney International*, and *Diabetes*.

Dr. Susztak's groundbreaking research has earned her a number of honors, including the ASN Barry M. Brenner, MD, Endowed Lectureship; the Alfred Newton Richards Award from the International Society of Nephrology; and the William Osler Patient Oriented Research Award from the Perelman School of Medicine. She is an elected member of The American Society for Clinical Investigation and the Association of American Physicians.

She received her medical and doctoral degrees from Semmelweis University in Budapest, Hungary. She then completed a residency in internal medicine and a fellowship in nephrology at the Albert Einstein College of Medicine, where she also earned a master's degree in clinical research.

Young Investigator Rafael Kramann Recognized for Work on Fibrosis

https://doi.org/10.62716/kn.001682025

Rafael Kramann, MD, PhD, FASN

The ASN-American Heart Association Donald W. Seldin Young Investigator Award will be presented to Rafael Kramann, MD, PhD, FASN, who will speak on "Cell by Cell, Space by Space: Unraveling Fibrosis in the Kidney and Heart" on Friday, November 7.

Dr. Kramann is a professor of medicine and chair of the Department of Medicine's Nephrology, Rheumatology, Immunology, and Hypertension specialties at Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen University in Aachen, Germany, where he also founded and directs the Center of Phase Transition in Chronic Disease.

He holds adjunct professorships at Erasmus Medical Center in Rotterdam, the Netherlands, and at the MDI (formerly Mount Desert Island) Biological Laboratory and The Jackson Laboratory, both located in Bar Harbor, ME. He also holds an honorary professorship at The University of Edinburgh, where he is principal investigator of the British Heart Foundation Centre of Research Excellence.

Dr. Kramann conducts research on chronic kidney disease, cardiovascular disease, and organ fibrosis (with a particular interest in kidney fibrosis), with the goal of understanding the mechanisms of disease and developing targeted therapies. He combines a range of research approaches, including multiomics, single-cell analysis, gene editing, genetic fate tracing, and ex vivo disease modeling. He has received numerous major research grants, including funding for a new facility in Aachen dedicated to fibrosis research, and has authored more than 200 scientific publications. He also holds several scientific leadership roles, including chair of the Kidney-Heart-Vasculature Board of the German Society of Nephrology and vice chair of the Scientific Advisory Board of the European Renal Association (ERA).

Dr. Kramann has cofounded two biotechnology companies focused on developing treatments for fibrosis. In 2023, he helped launch Sequantrix, which uses single-cell genomics and artificial intelligence to identify drug candidates for treating fibrosis. He also cofounded MatriTarg Laboratories, which won the Harvard University Innovation Lab Deans' Health and Life Sciences Challenge in 2013.

In recognition of his work, Dr. Kramann has received the Stanley Shaldon Award from ERA, the Theodor Frerichs Award from the German Society for Internal Medicine, and the Wilhelm Vaillant Award from the Wilhelm Vaillant Foundation. He is a member of The American Society for Clinical Investigation, an ERA distinguished fellow, and an ASN fellow.

Dr. Kramann completed his medical degree, followed by a residency and renal fellowship, at RWTH Aachen University. He then completed a postdoctoral research fellowship at Brigham and Women's Hospital, a teaching affiliate of Harvard Medical School. He also earned a PhD from Erasmus University, where he studied the cellular and molecular basis of organ fibrosis.

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.

Presented on Friday, November 7, these awards recognize up to three winners in each of five categories: clinical service, education, leadership, mentorship, and research.

Distinguished Clinical Service Award

https://doi.org/10.62716/kn.001522025

Daniel Y. Lam, MD

Dr. Lam is a clinical professor of medicine in the Division of Nephrology at the University of Washington in Seattle. He is also an attending physician at Harborview Medical Center, where he previously served as medical director for palliative care, director of the Harborview Medical Center's Palliative Care Outpatient Clinic, as well as palliative care medical advisor for Northwest Kidney Centers.

His leadership has helped improve access to palliative care for people receiving dialysis, which can include supporting management of symptoms, navigating multiple chronic conditions, making complex medical decisions, and planning for end-of-life care. In 2017, he helped establish the first palliative care program within a dialysis facility in the United States at Northwest Kidney Centers. The program grew to serve six dialysis facilities across the organization. His advocacy efforts have been instrumental in allowing patients in Washington to remain on dialysis after entering hospice care.

Through his work with the Nonprofit Kidney Care Alliance, Dr. Lam continues to pursue legislative and regulatory changes that enhance palliative care for people on dialysis. He also serves on the Coalition for Supportive Care of Kidney Patients Executive Committee and ASN's Policy and Advocacy Committee.

Dr. Lam received a Sojourns Scholar Leadership Program award from the Cambia Health Foundation in 2015 and was named an Emerging Leader in Hospice and Palliative Care by the American Academy of Hospice and Palliative Medicine in 2019.

He received his medical degree from Tufts University School of Medicine. He then completed an internal medicine residency, as well as fellowships in nephrology and palliative medicine, at the University of Washington.

Distinguished Clinical Service Award

https://doi.org/10.62716/kn.001842025

Shina Menon, MD, FASN

Dr. Menon is associate professor of pediatrics in the Division of Nephrology at Stanford Medicine, where she is also the director for research in Pediatric Nephrology. In addition, she serves as medical director of Pediatric Acute Dialysis Therapy at Lucile Packard Children's Hospital Stanford, CA. Before joining Stanford Medicine, Dr. Menon held faculty positions at the University of Washington and Seattle Children's Hospital.

Her research and clinical work focus on critical care nephrology and pediatric acute kidney injury (AKI). She is dedicated to improving outcomes after AKI, creating clinical decision support systems for treating AKI, and refining how continuous kidney replacement therapy is administered to infants and young children.

Dr. Menon served on the ASN AKINow Artificial Intelligence Workgroup, as well as the ASN Kidney Health Guidance Workgroup on Outpatient Dialysis for AKI. She is cochair of the American Society of Pediatric Nephrology's Acute Care Nephrology Interest Group, which provides resources on AKI and kidney replacement therapy to support the development of new treatment programs.

She has authored more than 100 peer-reviewed articles and 12 book chapters and serves on the editorial board of *Pediatric Nephrology*. She is a fellow of ASN.

Dr. Menon received her medical degree from Maulana Azad Medical College at the University of Delhi in India, where she also completed her residency. She then completed a pediatric residency and a fellowship in pediatric nephrology at Children's Hospital of Michigan. In addition, she trained in acute care nephrology through a fellowship at Cincinnati Children's Hospital Medical Center.

Distinguished Educator Award

https://doi.org/10.62716/kn.001492025

Benjamin S. Ko, MD

Dr. Ko is associate professor of medicine and associate program director of the Nephrology Fellowship Program in the Section of Nephrology at The University of Chicago Pritzker School of Medicine, IL. He also serves as director of the renal biopsy service and is a principal preceptor in the nephrology fellows' clinic at UChicago Medicine. In addition to these roles, he attends on both the general internal medicine and nephrology consultative services.

Dr. Ko's career has focused on medical education at both the institutional and national levels, with particular emphasis on making renal physiology accessible and engaging to learners. He is the lead faculty for ASN's Kidney TREKS (Tutored Research and Education for Kidney Scholars) course in Chicago, which fosters early interest in nephrology among medical and graduate students. He has served on ASN's Workforce and Training and Kidney Week Education committees, as well as the National Board of Medical Examiners Test Development and Materials Committee.

At the Pritzker School of Medicine, Dr. Ko directs the physiology course and has led a significant overhaul of its curriculum to better reflect the needs of modern learners. His excellence in education has been recognized with multiple teaching and mentorship awards. He is a fellow of the Academy of Distinguished Medical Educators.

Dr. Ko has authored several book chapters and society-sponsored guidelines and serves on the editorial boards of *Frontiers in Renal and Epithelial Physiology* and the *American Journal of Physiology-Renal Physiology*. He is a frequently invited speaker on topics related to workforce development and medical education.

Dr. Ko received his MD from the University of Illinois College of Medicine. He completed his residency in internal medicine through the Yale School of Medicine at Yale New Haven Hospital and his nephrology fellowship through the Pritzker School of Medicine at UChicago Medicine.

Distinguished Educator Award

https://doi.org/10.62716/kn.001552025

Hitesh H. Shah, MD, FASN

Dr. Shah is a professor of medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell in Hempstead, NY, and is senior director of nephrology education in the Division of Kidney Diseases and Hypertension at Northwell Health. He has served as director of the Nephrology Fellowship Program for 18 years and currently leads educational initiatives that have had a significant impact locally and nationally.

Dr. Shah is known for pioneering innovative nephrology educational programs, including Northwell's nephrology tracks within the general fellowship and novel elective experiences for medical students and residents that reflect clinical nephrology practice. His educational leadership and scholarship have been recognized through publications in high-impact journals such as the *American Journal of Kidney Diseases*, *CJASN*, and *JASN*.

Nationally, Dr. Shah has played an integral role in ASN's education efforts. He has served on numerous ASN committees, including the Workforce and Training Committee, Kidney STARS (Students and Residents), and Kidney TREKS (Tutored Research and Education for Kidney Scholars), and has helped create and moderate the Fellows-in-Training Bowl, a flagship ASN Kidney Week event. He is past president of The New York Society of Nephrology.

Dr. Shah has authored more than 85 peer-reviewed articles and 18 book chapters. He was recognized for his dedication to nephrology education with the 2021 Candee Award for Excellence in Education from the Northwell Health Department of Medicine.

Dr. Shah earned his medical degree from Jawaharlal Nehru Medical College in Belgaum, India. He completed an internal medicine residency at Flushing Hospital Medical Center in Queens, NY, and his nephrology fellowship at Long Island Jewish Medical Center, a part of Northwell Health, before joining the faculty.

Distinguished Leader Award

https://doi.org/10.62716/kn.001612025

Laura H. Mariani, MD, MS, FASN

Dr. Mariani is an associate professor of internal medicine in the Division of Nephrology at the University of Michigan Medical School and attending physician at University of Michigan Health in Ann Arbor. She is also assistant clerkship director for the internal medicine clerkship and assistant program director for the nephrology fellowship training program at the University of Michigan Medical School.

Her research and clinical work focus on glomerular diseases, as well as the application of statistical methods to identify therapeutic targets, search for novel biomarkers, and predict the progression of kidney diseases. Throughout her career, she has led numerous national and international translational efforts to improve care for kidney diseases, including the Proteinuria and GFR [Glomerular Filtration Rate] as Clinical Trial Endpoints in Focal Segmental Glomerulosclerosis project, which aims to accelerate trials for focal segmental glomerulosclerosis. She is principal investigator of the Cure Glomerulonephropathy consortium data coordinating center and an investigator in both the Nephrotic Syndrome Study Network and the Kidney Precision Medicine Project Central Hub.

Dr. Mariani is also dedicated to mentoring the next generation of nephrologists. She co-leads the Nephrotic Syndrome Study Network-Cure Glomerulonephropathy career enhancement program and is principal investigator for the Kidney, Urology, and Hematology Training Network at the University of Michigan.

She is a fellow of ASN and a member of the editorial boards of the *American Journal of Kidney Diseases* and *Kidney360*.

Dr. Mariani received her medical degree from the University of Michigan. At the University of Pennsylvania Perelman School of Medicine, she completed a residency in internal medicine, served as chief medical resident, and earned a master's degree in clinical epidemiology. She also completed fellowship training in nephrology at the Hospital of the University of Pennsylvania.

Distinguished Leader Award

https://doi.org/10.62716/kn.001722025

Reem A. Mustafa, MD, PhD, MPH, FASN

Dr. Mustafa is a professor of medicine in the Division of Nephrology and Hypertension at The University of Kansas Medical Center, Kansas City, where she also serves as director of the Agency for Healthcare Research and Quality-designated Evidence-Based Practice and Impact Center. A specialist in evidence-based medicine, she is known for her international leadership in developing and evaluating clinical practice guidelines that improve patient outcomes.

Dr. Mustafa's work integrates internal medicine, nephrology, and public health with a research focus on diagnostic decision-making and the application of evidence-based methods to both clinical and population health. She has led guideline development for the World Health Organization, the Infectious Diseases Society of America, the American Society of Hematology, and the Canadian Society of Nephrology, among others. She chairs the methods committee and serves on the executive committee for Kidney Disease: Improving Global Outcomes (KDIGO) and is cofounder of both the US GRADE [Grading of Recommendations Assessment, Development and Evaluation] Network and the Evidence Foundation.

A recognized leader in medical research, Dr. Mustafa has authored more than 350 peer-reviewed publications and serves as a member of the GRADE guidance group's executive committee. From 2021 to 2023, she was named a top 1% most-cited researcher by Clarivate for her high-impact work across disciplines.

Her leadership is matched by her commitment to education and mentorship. She received the Outstanding Research Mentorship Award from The University of Kansas Health System and has been honored multiple times for excellence in teaching and clinical instruction.

Dr. Mustafa earned her medical degree from The University of Jordan School of Medicine. She completed residency in internal medicine and preventive medicine, a fellowship in nephrology, and a Master of Public Health degree at the University of Buffalo, The State University of New York. She also holds a PhD in health research methodology from McMaster University in Hamilton, Ontario, Canada.

Distinguished Mentor Award

https://doi.org/10.62716/kn.001572025

Julia J. Scialla, MD, MHS, FASN

Dr. Scialla is an associate professor of medicine and public health sciences at the University of Virginia (UVA) School of Medicine, Charlottesville. She serves as director of the Nephrology Clinical Research Center and director of outcomes research in the Departments of Medicine and Public Health Sciences. She is also an Executive Committee member for the UVA Physician Scientist Training Program and holds leadership roles in multiple National Institutes of Health-funded training networks.

A dedicated mentor and educator, Dr. Scialla has played a central role in shaping the next generation of kidney researchers. She directs clinical integration efforts for the Integrated Virginia Research Training Centers in Kidney, Urology and Hematology training network and serves on the internal advisory board for the Virginia Kidney Technology Development Research Education Program. She has been recognized for her contributions with UVA's Department of Medicine Excellence in Mentoring Award and Teaching Excellence Award from the Division of Nephrology.

Additionally, Dr. Scialla is deputy editor of the *American Journal of Kidney Diseases* and has served on the editorial board for *CJASN*. She is an active member of the National Kidney Foundation, currently serving on its scientific advisory board and as program cochair for the 2025 and 2026 Spring Clinical Meetings. In 2023, she was an invited participant at the Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference on chronic kidney disease–mineral and bone disorder.

Dr. Scialla's research focuses on chronic kidney disease epidemiology, with an emphasis on secondary prevention, mineral and bone complications, and data science. She has authored nearly 100 peer-reviewed publications, as well as numerous invited reviews and editorials.

Dr. Scialla earned her MD from the University of Pennsylvania Perelman School of Medicine. She completed her internal medicine residency and nephrology fellowship at The Johns Hopkins Hospital, affiliated with the Johns Hopkins School of Medicine. She also earned a Master of Health Science degree in clinical epidemiology from the Johns Hopkins Bloomberg School of Public Health.

Distinguished Researcher Award

https://doi.org/10.62716/kn.001482025

Aminu K. Bello, MD, PhD, FASN

Dr. Bello is a professor of medicine at the University of Alberta in Edmonton, Canada. He is also medical director for the dialysis unit at the Peace River Community Health Centre and attending physician at the University of Alberta Hospital, both part of Alberta Health Services. In addition, he is adjunct professor of medicine at the Alberta Diabetes Institute of the University of Alberta and an honorary professor of medicine in the Division of Nephrology and Hypertension, Department of Medicine, at the University of Cape Town in South Africa.

Dr. Bello is dedicated to improving nephrology education and practice through global health initiatives. He is cochair for the Global Kidney Health Atlas of the International Society of Nephrology, which evaluates the capacity for kidney care worldwide. His leadership of the project has led to collaborations across 164 countries and a series of policy briefs, which have been widely adopted by international nephrology societies to guide the prevention and treatment of chronic kidney disease and acute kidney injury. In Canada, his research has helped build capacity to treat chronic kidney disease and monitor its risk factors in remote, rural, and Indigenous communities.

In 2023, he was inducted into the Canadian Academy of Health Sciences. He is also a fellow of The African Academy of Sciences and ASN and is a Killam Laureate.

In Nigeria, Dr. Bello received his medical degree from Usmanu Danfodiyo University, Sokoto, and underwent residency training in general internal medicine at the University College Hospital, Ibadan. He then completed specialty training and earned his PhD in nephrology and epidemiology at The University of Sheffield in the United Kingdom. He also completed a clinical fellowship in nephrology and transplantation, as well as a nephrology research fellowship, at the University of Alberta.

Distinguished Researcher Award

https://doi.org/10.62716/kn.001532025

Elaine Ku, MD, FASN

Dr. Ku is an associate professor in residence in the Departments of Medicine, Pediatrics, and Epidemiology and Biostatistics at the University of California San Francisco (UCSF) School of Medicine. In her role, she directs the Advanced Training in Clinical Research certificate program, the Master's Degree in Clinical and Epidemiologic Research, and the MATCH (Multi-Disciplinary Advancement of Transplant-Centered Health) Outcomes Research Center. In addition, she leads the Nephrology Transition Clinic at UCSF Health.

Dr. Ku's research focuses on understanding differences in the epidemiology, clinical management, and outcomes of children and adults with kidney diseases, particularly in the context of care transitions, from adolescence to young adulthood and from advanced chronic kidney disease to kidney failure. Her National Institutes of Health (NIH)-funded work explores barriers to kidney transplantation and strategies to optimize management of cardiovascular comorbidities, such as hypertension and obesity, in people with kidney diseases.

She has served on NIH study sections and ASN's Grant Review Committee, and she is currently an associate editor for the *American Journal of Kidney Diseases*. Dr. Ku is also actively engaged in leadership roles within national organizations, including serving as a section lead for the National Kidney Foundation's Working Group on Mental and Behavioral Health and as a member of Kidney Disease: Improving Global Outcomes (KDIGO) work groups.

Dr. Ku has authored more than 100 peer-reviewed articles and contributed to nine book chapters. She is a fellow of ASN and was elected to The American Society for Clinical Investigation in 2023. Her recent honors include the Distinguished Visiting Professorship at Baylor College of Medicine and the David Cornfeld Lectureship at Children's Hospital of Philadelphia.

Dr. Ku earned her MD from the UC San Diego School of Medicine and completed residency training at the Los Angeles County Medical Center (now Los Angeles General Medical Center) through the Keck School of Medicine of the University of Southern California. She completed adult and pediatric nephrology fellowships at the UCSF School of Medicine, where she has been a faculty member since 2015.

Distinguished Researcher Award

https://doi.org/10.62716/kn.001852025

Simone Sanna-Cherchi, MD

Dr. Sanna-Cherchi is associate professor of medicine in the Division of Nephrology at Vagelos College of Physicians and Surgeons at Columbia University Irving Medical Center in New York City. A leader in genetic kidney disease research, he is internationally recognized for his work in uncovering the molecular basis of disorders such as congenital abnormalities of the kidney and urinary tract and nephrotic syndrome.

Dr. Sanna-Cherchi's research brings together investigators across disciplines and continents to study complex, understudied kidney conditions. He has led large-scale collaborative projects supported by the National Institutes of Health, the US Department of Defense, ASN, and other major funders. His studies have appeared in high-impact journals including *The New England Journal of Medicine*, *Science*, *Nature Genetics*, *Nature Communications*, and *The Journal of Clinical Investigation*. He currently serves as associate editor for both *Glomerular Diseases* and *JASN*.

He has authored more than 80 peer-reviewed publications and serves as an organizer of the Division of Nephrology Grand Rounds in basic research at Columbia University.

In recognition of his scientific contributions and collaborative leadership, Dr. Sanna-Cherchi was elected a member of The American Society for Clinical Investigation in 2018 and was a founding elected member of the International Society of Glomerular Disease in 2023. He has delivered keynote and invited lectures around the world, including the David Cornfeld Lecture in Nephrology at the Children's Hospital of Philadelphia and the Henry Shavelle Visiting Professorship in Nephrology in Los Angeles.

Dr. Sanna-Cherchi received his medical degree and completed a residency and fellowship in internal medicine and nephrology at the University of Parma Faculty of Medicine and Surgery in Italy. He also finished a postdoctoral fellowship in nephrology and genetics at Columbia University. In addition, he achieved an internal medicine residency at St. Luke's Roosevelt Hospital Center (now Mount Sinai Morningside–Mount Sinai West), through the Icahn School of Medicine at Mount Sinai. Dr. Sanna-Cherchi later completed a nephrology fellowship at Columbia University, before joining the faculty in 2015.

Vasculitis Pioneer to Share Lessons From Long-Term Patient Remission

https://doi.org/10.62716/kn.001832025

Ronald J. Falk, MD, FASN

An internationally recognized physician-scientist will deliver the Robert W. Schrier, MD, Endowed Lectureship on Friday, November 7, during the session "Changing Landscape for Management of Vasculitis." Ronald J. Falk, MD, FASN, will present a lecture titled "ANCA-Associated Vasculitis: Lessons Learned From Patients in Long-Term Remission Off Therapy."

Dr. Falk is professor of medicine at The University of North Carolina (UNC) at Chapel Hill and cofounder and director of the UNC Kidney Center. A leader in nephrology for more than 3 decades, at UNC, he previously served as chief of the Division of Nephrology and Hypertension from 1993 to 2015 and chair of the Department of Medicine from 2015 to 2025. He is a fellow of both the American College of Physicians and ASN.

Dr. Falk's research has helped shape understanding of the causes, mechanisms, and clinical progression of autoimmune kidney diseases, with a particular focus on the genetics of and biomarkers for antineutrophil cytoplasmic autoantibody-associated vasculitis. He holds seven patents for new methods to detect and monitor these kidney disease biomarkers. He has coauthored more than 300 peer-reviewed journal articles and 100 book chapters and has served as editor of seven books. He has also served on the editorial boards of several leading publications, including *JASN*, *Kidney International*, and the American College of Physicians' Medical Knowledge Self-Assessment Program series.

Since 1997, Dr. Falk has served on numerous National Institutes of Health study sections and steering committees, helping guide national research strategy in kidney diseases and immunology. Within ASN, he has held multiple leadership roles, including serving as president from 2011 to 2012. During his presidency, he founded the Kidney Health Initiative, a public–private partnership with the US Food and Drug Administration. A committed advocate for collaborative science, Dr. Falk cofounded the UNC Glomerular Disease Collaborative Network in 1985. Today, this network includes more than 600 nephrologists from more than 250 clinics across eight states. Under his leadership, UNC serves as one of four clinical centers in the national Cure Glomerulonephropathy consortium, focused on long-term data gathering to advance glomerular disease research.

In recognition of his contributions, Dr. Falk has received numerous honors and awards, including the John P. Peters Award for lifetime achievement from ASN in 2017, the Edward N. Gibbs Award and Lecture in Nephrology from The New York Academy of Medicine in 2016, and election to the ASN Council in 2006. He has also held several distinguished professorships at UNC, most recently awarded the first Nan and Hugh Cullman Eminent Professor.

He earned his medical degree from the UNC School of Medicine, where he also completed his residency in internal medicine and a fellowship in nephrology. He achieved a fellowship in pediatric nephrology at the University of Minnesota Hospitals in Minneapolis, now named the M Health Fairview University of Minnesota Medical Center.

Murphy Lectureship to Focus on Considerations for Living Donation

https://doi.org/10.62716/kn.001752025

Robert S. Gaston, MD

A distinguished expert in living donor kidney transplantation will deliver the Barbara T. Murphy, MB BAO BCh, Endowed Lectureship on Friday, November 7. Robert S. Gaston, MD, will speak on "Challenging the Status Quo in Living Donation: Controversial Medical and Ethical Considerations."

Dr. Gaston is professor emeritus in the Division of Nephrology at The University of Alabama at Birmingham (UAB) Marnix E. Heersink School of Medicine. He recently completed a 7-year tenure as senior medical director at CTI Clinical Trial and Consulting Services, where he played a central role in developing new therapeutic approaches in nephrology and transplantation.

After joining the full-time faculty of UAB in 1990, Dr. Gaston helped spearhead the growth of the institution's kidney transplant program. He served as the program's medical director, as well as the director of the Comprehensive Transplant Institute. He also held the position of vice president for transplant services and was the inaugural holder of the Robert G. Luke, MD, Endowed Chair in Transplant Nephrology at UAB.

A recognized leader in living donor kidney transplantation, Dr. Gaston has authored or coauthored more than 300 publications. His research has focused on kidney transplant outcomes, including late allograft failure and nephrotoxicity, as well as outcomes and risk factors for living donors. He has also investigated how to optimize immunosuppressive therapy, as well as genetic, cardiovascular, and immunological factors that influence the success of transplantation. He has served on numerous national and regional committees related to transplantation, including for the US Food and Drug Administration, the American Society of Transplantation, the Scientific Registry of Transplant Recipients, and other organizations.

His work has earned him several honors, including a Lifetime Achievement Award from the American Society of Transplantation, where he also served as president during the 2011–2012 term. At UAB, he was selected for the Healthcare Leadership Academy in 2010 and delivered the Thomas E. Andreoli Lecture in 2016.

Dr. Gaston received his medical degree from the Saint Louis University School of Medicine, MO. He then completed a residency in internal medicine and a fellowship in nephrology at the University of Arkansas for Medical Sciences, Little Rock. Before joining the faculty at UAB, he trained as the university's first fellow in renal transplant nephrology.

Health Disparities Leader to Speak on Race and Ethnicity in Kidney Medicine

https://doi.org/10.62716/kn.001602025

Keith C. Norris, MD, PhD

An internationally renowned health policy expert and clinician scientist will deliver the Christopher R. Blagg, MD, Endowed Lectureship in Kidney Diseases and Public Policy on Friday, November 7. Keith C. Norris, MD, PhD, will speak on "Best Practices for Integrating Race, Ethnicity, and Ancestry in Kidney Care and Research."

Dr. Norris is professor of medicine and executive vice chair for Community Engagement and Inclusive Excellence in the Department of Medicine at University of California, Los Angeles (UCLA) Health. He also serves as codirector of the Community Engagement and Research Program at the UCLA Clinical and Translational Science Institute, which connects community members, researchers, and policymakers to improve health across Los Angeles.

Dr. Norris' research and leadership have helped shape clinical practice guidelines and national health policy for chronic kidney disease. He was selected to join the inaugural National Kidney Foundation Dialysis Outcomes Quality Initiative in 1995 (renamed the Kidney Disease Outcomes Quality Initiative), where he worked to improve Medicare guidelines for people living with chronic kidney disease. Today, he leads six National Institutes of Health (NIH)-funded research and training grants and has coauthored more than 550 peer-reviewed journal articles and 30 book chapters.

Throughout his career, health disparities have been a major focus of his work. He was a member of the pilot study for the African American Study of Kidney Disease and Hypertension and a principal investigator for both the full study and the cohort follow-up study. He was also the founding principal investigator for the NIH–Research Centers in Minority Institutions Translational Research Network, the first translational research network aimed at reducing health disparities, funded by NIH.

Dr. Norris has spearheaded several efforts to improve community-academic partnerships. In 2009, he codeveloped a Community Faculty Track at the Charles R. Drew University of Medicine and Science to help infuse community voices into health education and research. He has worked extensively to recruit and retain patients in the South Los Angeles area and leads several NIH training efforts to improve diversity in the health sciences.

Dr. Norris has received many honors and awards in recognition of his contributions, including election to the National Academy of Medicine, fellowship in both ASN and the American College of Physicians, and induction into the National Black College Alumni Hall of Fame Foundation. He currently serves on the American Association of Kidney Patients Medical Advisory Board and The National Forum of End Stage Renal Disease Networks Medical Director Advisory Council. He is editor-in-chief emeritus of *Ethnicity & Disease*, an international journal focused on the intersection of ethnicity, health disparities, and disease outcomes.

He received his medical degree from Howard University College of Medicine, followed by an internal medicine residency, where he was chief resident. He then completed a nephrology fellowship through the combined West Los Angeles Veterans Affairs–UCLA program. In 2014, he earned a PhD in religious, spiritual, and metaphysical philosophy from The College of Metaphysical Studies in Clearwater, FL.

KIDNEY WEEK 2025

November 5–9 | Houston, TX

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PLENARY SESSION

STATE-OF-THE-ART LECTURES

Global Biotechnology Leader to Deliver Plenary on Drug Development

https://doi.org/10.62716/kn.001732025

Reshma Kewalramani, MD, FASN

Reshma Kewalramani, MD, FASN, will deliver a state-of-the-art lecture titled "On Kidney Medicine, Drug Development, and Coming Home" at a plenary session on Saturday, November 8.

Dr. Kewalramani is chief executive officer (CEO) and president of Vertex Pharmaceuticals, a global biotechnology company. After joining Vertex Pharmaceuticals in 2017, she served as chief medical officer and executive vice president of global medicines development and medical affairs before becoming CEO in 2020.

Vertex Pharmaceuticals has developed and received US Food and Drug Administration (FDA) approval for five medications that treat cystic fibrosis. The company has also gained FDA approval for a gene-edited therapy for people living with sickle cell disease and transfusion-dependent beta thalassemia, as well as a nonopioid pain medication. Additional therapeutics are being developed to treat pain, cystic fibrosis, type 1 diabetes, myotonic dystrophy type 1, and several kidney diseases: apolipoprotein L1-mediated kidney disease, autosomal dominant polycystic kidney disease, and immunoglobulin A nephropathy.

In addition to her leadership in pharmaceutical discovery, Dr. Kewalramani is dedicated to fostering scientific talent and supporting medical institutions. She serves on the boards of directors for Year Up United and the Biomedical Science Careers Program, two nonprofit companies focused on education and career development for underserved individuals. She is also on the Massachusetts General Hospital Board of Trustees and the Boston University Chobanian & Avedisian School of Medicine Dean's Advisory Board.

Dr. Kewalramani has earned numerous honors for her scientific leadership, including the Distinguished Alumni Award from the Boston University Chobanian & Avedisian School of Medicine, the Harvard Business School Alumni Achievement Award, the Asian American Business Development Center Pinnacle Award, and ASN fellowship. In 2021, she received the New Englander of the Year Award from the New England Council and the Golden Door Award from the International Institute of New England. She was named one of *TIME*'s TIME100 Most Influential People of 2025, one of *Fortune*'s 2025 Most Powerful Women, and a *Barron's* 2024 Top CEO.

She received her medical degree from the Boston University Chobanian & Avedisian School of Medicine and then did her residency in internal medicine at Massachusetts General Hospital. She then completed the Brigham and Women's Hospital/Massachusetts General Hospital Joint Nephrology Fellowship program and the General Management Program at Harvard Business School.

Social Work Scholar to Speak on Building Resilience

https://doi.org/10.62716/kn.001642025

Michael Ungar, PhD

A world-renowned social work scholar will deliver a state-of-the-art lecture on how understanding resilience can improve patient care. At a plenary on Saturday, November 8, Michael Ungar, PhD, will discuss "Resilience at Work and at Home: Finding the Rugged Qualities and Collective Resources We Need."

Dr. Ungar is a family therapist and professor of social work at Dalhousie University in Halifax, Nova Scotia, Canada, where he directs the Resilience Research Centre, which conducts longitudinal research focused on marginalized children, adults, and families across more than one dozen countries. He also holds the Canada Research Chair in Child, Family and Community Resilience.

He has studied resilience in cultures around the world, making such a substantial contribution to his field that he was identified as the top contributor to social work scholarship globally. Dr. Ungar's work on psychosocial resilience has important implications for nephrology. His research focuses on how individuals and communities adapt to adversity through access to external supports such as strong relationships, stable environments, and responsive systems.

People living with chronic kidney disease, on dialysis, or recovering from transplant face complex treatment plans, unpredictable medical complications, and major disruptions to daily life. Ungar's work suggests that building resilience in these conditions depends on structures that support patients' complex emotional, social, and practical needs. This includes coordinated care teams, family education, mental health support, and access to community-based services.

Bringing psychosocial resilience frameworks into nephrology can help clinicians and researchers better understand what helps patients adapt to chronic illness. Ungar's insights highlight the need for a holistic approach to kidney care, which considers not just medical outcomes but also the social and emotional scaffolding that makes those outcomes possible.

Dr. Ungar has authored 18 books on his approaches to resilience for use by mental health professionals, employers, educators, and caregivers. These include *Working With Children and Youth With Complex Needs: 20 Skills to Build Resilience*; *Change Your World: The Science of Resilience and the True Path to Success*; and *The Limits of Resilience: When to Persevere, When to Change, and When to Quit*, books to support organizations and to help individuals experiencing stress. He has also published more than 180 peer-reviewed journal articles and book chapters focused on resilience. In addition, Dr. Ungar maintains a *Psychology Today* blog, "Nurturing Resilience," in which he shares insights on parenting, current events, and other subjects.

He has received a number of awards for his work, including the National Award for Outstanding Service from the Canadian Association of Social Workers. In 2018, he was named a fellow of the Royal Society of Canada. Dr. Ungar received his doctoral degree in social work from Wilfrid Laurier University in Waterloo, Ontario, Canada, with a focus on family therapy, research methods, and resilience.

Former FDA Commissioner and Renowned Clinical Researcher to Receive President's Medal

https://doi.org/10.62716/kn.001742025

Robert M. Califf, MD

Former head of the US Food and Drug Administration (FDA) and distinguished cardiovascular medicine researcher Robert M. Califf, MD, will receive the ASN President's Medal on Saturday, November 8, in recognition of his contributions to clinical research and evidence-based health policy at the national level.

ASN presents this medal to individuals who have advanced the society's mission to fight against kidney diseases by educating health professionals, sharing new knowledge, advancing research, and advocating for patients.

Dr. Califf served as commissioner of food and drugs from 2016 to 2017 and from 2022 to 2025. He stepped down in March 2025. As FDA's top official, he worked to improve the efficiency and inclusivity of clinical trials, advance tobacco regulation, strengthen drug approval and oversight, and prepare the agency to respond to health emergencies. He was the agency's deputy commissioner for medical products and tobacco from 2015 to 2016.

Dr. Califf is also adjunct professor of medicine at the Duke University School of Medicine, Durham, NC, where he previously held the roles of professor of medicine, vice chancellor for clinical and translational research, director of the Duke Clinical & Translational Science Institute, and founding director of the Duke Clinical Research Institute. Between his terms as FDA commissioner, he was head of medical strategy and senior adviser at Alphabet Inc., where he provided strategic leadership for Verily Life Sciences (now called Verily) and Google Health (now called Google for Health).

He has published more than 1300 peer-reviewed articles, including many seminal clinical trials, and is one of the most cited authors in biomedical science. His research has focused on cardiovascular health, such as enhancing acute care for people having a heart attack, as well as improving health outcomes and quality of care for diverse populations. Dr. Califf has also led several efforts to improve the quality and efficiency of clinical trials. He cofounded the Clinical Trials Transformation Initiative, a public-private partnership between FDA and Duke that unites regulators, academics, industry leaders, and patient advocates to find practical solutions to pressing challenges in clinical research.

In 2016, Dr. Califf was inducted into the National Academy of Medicine. He has served on numerous advisory committees for institutes and centers at the National Institutes of Health, including for the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute of Environmental Health Sciences; and the National Library of Medicine.

He received his medical degree from the Duke University School of Medicine, where he later completed fellowship training in cardiology. He completed his residency in internal medicine at University of California San Francisco (UCSF) Health, affiliated with the UCSF School of Medicine.

Biff F. Palmer to Receive Robert G. Narins Award for Contributions in Education

https://doi.org/10.62716/kn.001502025

Biff F. Palmer, MD, FACP, FASN

Biff F. Palmer, MD, FACP, FASN, will receive the Robert G. Narins Award on Saturday, November 8, for his extensive contributions in educating and training the next generation of nephrologists.

Dr. Palmer is a professor of education and internal medicine at the Texas Tech University Health Sciences Center El Paso Paul L. Foster School of Medicine. He maintains an adjunct professorship at The University of Texas (UT) Southwestern Medical Center, where he was professor of internal medicine for 35 years. He also continues to lead medical student education at The UT Southwestern Medical Center, focusing on renal and genitourinary systems.

Throughout his career, Dr. Palmer has dedicated himself to training nephrologists at every level, including medical students, residents, fellows, and practicing physicians. He mentors medical students on professionalism, ethics, and other topics and aids in the development of medical school curricula. He was recruited in 2024 by the Paul L. Foster School of Medicine, which is part of the Texas Tech University System that predominantly serves students from underrepresented populations. In his new position, he mentors students and shapes medical education programs, continuing his lifelong commitment to medical training and expanding his impact in a new institutional setting.

In addition to his work as an educator, Dr. Palmer has authored more than 310 peer-reviewed articles and chapters focused on nephrology, metabolism, and endocrinology. At The UT Southwestern Medical Center, he held a number of leadership positions, including director of clinical nephrology, acting chief of the Division of Nephrology, program director for the Nephrology Fellowship Program, and associate training program director for internal medicine. He is associate editor of the *American Journal of Nephrology* and serves on the editorial boards of *Clinical Nephrology* and the *American Journal of Kidney Diseases*.

Dr. Palmer has earned several outstanding teaching awards at The UT Southwestern Medical Center, including the Regents Outstanding Teaching Award and the title of distinguished teaching professor. He is an elected member of the Kenneth I. Shine, MD, Academy of Health Science Education and The UT Southwestern Academy of Teachers. He has also received the Piper Professor Award from the Minnie Stevens Piper Foundation and the Distinguished Biomedical Science Educator Award from The UT Southwestern Academy of Teachers, among other honors. He is a fellow of ASN and the American College of Physicians.

Dr. Palmer earned his medical degree from The UT Southwestern Medical Center and then completed a residency in internal medicine and a research fellowship in nephrology at Walter Reed Army Medical Center, now Walter Reed National Military Medical Center. He also completed a clinical fellowship in nephrology at The UT Southwestern Medical Center-Parkland Memorial Hospital.

Transplant Nephrology Leader to Receive Barbara T. Murphy Award

https://doi.org/10.62716/kn.001662025

Michelle A. Josephson, MD, FASN

ASN will present the Barbara T. Murphy Award to Michelle A. Josephson, MD, FASN, on Saturday, November 8. This award is named for the distinguished nephrologist and late ASN president-elect. It honors leaders who strengthen the foundation of nephrology while advancing the field through innovation, creativity, inspiration, and tenacity.

Dr. Josephson is professor of medicine and surgery at The University of Chicago Pritzker School of Medicine, IL. She is director of education for The University of Chicago Medicine Transplant Institute and program director for the Training Program in Transplant Nephrology, the first kidney transplant fellowship in Illinois, which she founded. She also launched The University of Chicago's kidney and pancreas transplantation program in 1992 and served as its medical director until 2023. She built a robust clinical and academic program from the ground up, carefully integrating patient care, research, and education in transplantation.

She has devoted her career to strengthening transplant nephrology care, education, research, and policy, both at her institution and at the national and international levels. That began during her early career, when she worked to address unmet needs in kidney transplant care. Her research has also advanced the understanding of post-transplant bone disease, pregnancy after kidney transplant, and BK virus nephropathy.

Dr. Josephson has held multiple roles at ASN, including president, using her tenure to improve transplant policy and training nationwide. She has also served as ASN secretary, chair of the Policy and Advocacy Committee, and member of the *CJASN* editorial board. She has held leadership roles in many other organizations, including serving as president of Women in Nephrology, councilor-at-large for the American Society of Transplantation (AST) board of directors, and member of the Kidney Disease: Improving Global Outcomes (KDIGO) board of directors and executive committee, among others. She is currently a member of the steering committee for ASN's Humanitarian Kidney Support Program and a representative for The Transplantation Society on the International Society of Nephrology–The Transplantation Society Sister Transplant Centers program committee.

Dr. Josephson has received a number of awards for her contributions, including the Michael Reese Lectureship Distinguished Faculty Award from the Biological Sciences Division at The University of Chicago. In 2019, she received the AST Mentoring Award, and in 2022, she received the Richard Yu Endowment Fund Award from the Hong Kong Society of Nephrology. She is a fellow of both AST and ASN.

She earned her medical degree from the Perelman School of Medicine at the University of Pennsylvania, Philadelphia. At The University of Chicago Pritzker School of Medicine, she completed her residency, as well as fellowships in both clinical and research nephrology and the MERITS (Medical Education Research, Innovation, Teaching, and Scholarship) Fellowship.

ASN to Bestow Belding H. Scribner Award on Michael Allon

https://doi.org/10.62716/kn.001632025

Michael Allon, MD

The Belding H. Scribner Award will be tendered on Saturday, November 8, to Michael Allon, MD, for his career-long contributions to the practice of nephrology.

Dr. Allon is a professor of medicine in the Division of Nephrology at the Heersink School of Medicine at The University of Alabama at Birmingham, where he also serves as the associate director for clinical affairs and the medical director of dialysis operations.

Established in 1995, the Belding H. Scribner Award is presented to individuals who have made outstanding contributions to the care of people with kidney disorders or have substantially influenced the clinical practice of nephrology. Dr. Allon is receiving the award because of his critical impact on kidney disease care, particularly for people receiving hemodialysis.

Throughout his career, Dr. Allon has been the principal investigator for a number of key clinical dialysis trials funded by the National Institutes of Health (NIH). His work has focused on dialysis vascular access, about which he has published more than 100 peer-reviewed articles, as well as a number of reviews and editorials, which have significantly enhanced the field's understanding. His landmark studies have spurred major advances in vascular access for dialysis, including pioneering the use of preoperative ultrasound vascular mapping and leading the shift toward patient-specific decisions about whether to use arteriovenous fistulas or arteriovenous grafts.

Dr. Allon has served as a member of multiple major scientific advisory boards and guideline committees focused on vascular access, including for ASN; the National Kidney Foundation; the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH; and the Centers for Medicare & Medicaid Services. He was chair of the Planning Committee for the NIDDK Hemodialysis Vascular Access Roundtable and for the Vascular Access Project Committee of Nephrologists Transforming Dialysis Safety. He is the inaugural editor-in-chief of *Kidney360*, for which he will conclude his term at the end of this year, and previously served as associate editor of *CJASN*.

Dr. Allon received his medical degree from the University of Michigan Medical School. He completed a residency in internal medicine and a fellowship in nephrology at the Emory University School of Medicine.

Eknoyan Lectureship to Cover KDIGO Guidelines for CKD

https://doi.org/10.62716/kn.001562025

Ian de Boer, MD, MS

"KDIGO Guidelines Decoded: What They Mean for CKD Management in Practice" is the title of the Garabed Eknoyan, MD, Endowed Lectureship, which will be delivered on Saturday, November 8.

The speaker will be Ian de Boer, MD, MS, professor of medicine, director of the Kidney Research Institute, director of research in nephrology, Joseph W. Eschbach Endowed Chair in Kidney Research, and adjunct professor of epidemiology in the Department of Medicine at the University of Washington School of Medicine, Seattle. Dr. de Boer also provides care for people with a wide spectrum of acute and chronic kidney conditions as an attending physician in nephrology with the VA Puget Sound Health Care System.

His research centers on the origins and clinical outcomes of diabetic kidney disease, using methods ranging from large epidemiologic studies to clinical trials. He has published extensively on the prevention, early intervention, and treatment of chronic kidney disease (CKD) in patients with diabetes. Other topics of interest include altered metabolic function in CKD and the role of vitamin D and mineral homeostasis in CKD and other conditions. He has coauthored more than 400 peer-reviewed articles.

Dr. de Boer has made substantial contributions to the translation of research into practice guidelines for CKD clinical care. He served on the Professional Practice Committee of the American Diabetes Association, where he helped review and update the *Standards of Medical Care in Diabetes*. As cochair of the Kidney Disease: Improving Global Outcomes [KDIGO] Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease, he organized a working group with perspectives from six continents and six specialties relevant to diabetic kidney disease. He has also served as deputy editor of *CJASN* and a member of several scientific review groups at the National Institutes of Health, which focused on kidney precision medicine and other topics.

His work has earned him several awards, including an ASN Distinguished Researcher Award, a Rising Star Award from the University of Washington Diabetes Research Center, and induction into The American Society for Clinical Investigation.

Dr. de Boer received his medical degree from the Oregon Health & Science University School of Medicine, followed by an internal medicine residency at University of California San Francisco Health. He completed clinical and research fellowships in nephrology, as well as a master's degree in epidemiology, at the University of Washington.

Cardiorenal Disease Leader to Speak on Iron-Induced Hypophosphatemia

https://doi.org/10.62716/kn.001672025

Myles Wolf, MD, MS, MSc

An international leader in mineral metabolism and cardiorenal disease will deliver the Jack W. Coburn, MD, Endowed Lectureship on Saturday, November 8. Myles Wolf, MD, MS, MSc, will speak on "Iron-Induced Hypophosphatemia: A Still Unrecognized Complication of Iron Replacement."

Dr. Wolf is the Sanford I. Weill Chair of Medicine in the Joan and Sanford I. Weill Department of Medicine at Weill Cornell Medicine and physician-in-chief at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York City. Over the past 2 decades, Dr. Wolf has held leadership roles at Harvard Medical School, the University of Miami Leonard M. Miller School of Medicine, Northwestern University Feinberg School of Medicine, and Duke University School of Medicine, where he served as chief of the Division of Nephrology and built interdisciplinary translational research programs.

Dr. Wolf's work has significantly advanced the field's understanding of fibroblast growth factor 23 (FGF23) in kidney diseases, mineral metabolism, and cardiovascular risk. His landmark discovery was the identification of bone-derived hormone FGF23 as a predictor of cardiovascular events and mortality in people with chronic kidney disease (CKD). His foundational work has reshaped the understanding of CKD-related mineral metabolism and is widely recognized in medical textbooks and board exams.

He led translational, epidemiologic, and laboratory-based studies and clinical trials to unveil molecular mechanisms linking FGF23 to cardiovascular outcomes. His research has led to new therapeutic targets (e.g., phosphate binders, FGF23 modulation) to improve cardiovascular outcomes in CKD. Dr. Wolf's team combines physiologic and interventional patient-oriented studies, population-based epidemiologic studies, clinical trials, and laboratory-based studies in a collaborative translational approach.

Among Dr. Wolf's more than 300 publications are original research reports in *The New England Journal of Medicine*, *JAMA*, *Nature Medicine*, the *Journal of Clinical Investigation*, *Circulation*, *Cell Metabolism*, and leading nephrology journals.

In every phase of his career, Dr. Wolf has been deeply committed to mentoring and training the next generation of nephrologist-scientists, embedding trainees across his research enterprise. His impact on the field is broad, deep, and ongoing. He is recognized as a strong mentor who directed physician-scientist training at Northwestern and Duke, supporting numerous fellows, students, and postdoctoral researchers over the years.

In recognition of his scientific contributions, Dr. Wolf received the ASN–American Heart Association Donald W. Seldin Young Investigator Award in 2014. He is a member of several professional organizations, including The American Society for Clinical Investigation, the Association of American Physicians, and the American Clinical and Climatological Association.

Dr. Wolf received his medical degree from The State University of New York (SUNY) Downstate Health Sciences University, Brooklyn; completed internal medicine and nephrology training at Massachusetts General Hospital, Boston; and obtained a master's degree in Clinical and Physiological Investigation from Harvard Medical School, Boston.

Critical Care Nephrologist to Discuss Strategies to Protect the Kidney in AKI

https://doi.org/10.62716/kn.001622025

Marlies Ostermann, MD, PhD

An internationally recognized leader in critical care nephrology will deliver the Burton D. Rose, MD, Endowed Lectureship on Saturday, November 8, during the session "Therapeutics in AKI: From Bench to Bedside." Marlies Ostermann, MD, PhD, will present a lecture titled "Delayed Remote Ischemic Preconditioning: Extending the Window for AKI Protection."

Dr. Ostermann is professor of intensive care and nephrology at Guy's and St Thomas' NHS Foundation Trust in London, England, where she leads research efforts focused on acute kidney injury (AKI), kidney replacement therapy, and extracorporeal blood purification in patients who are critically ill. She is president-elect of the European Society of Intensive Care Medicine and serves as director of research for the Intensive Care Society (UK). She is a fellow of the Royal College of Physicians, London.

A recognized authority in AKI and sepsis, Dr. Ostermann cochairs the Kidney Disease: Improving Global Outcomes (KDIGO) AKI guideline committee and serves on the guideline panel of the Surviving Sepsis Campaign. Her research has significantly advanced understanding of AKI physiology and immunobiology, the role of biomarkers in diagnosis and prognosis, and therapeutic strategies for kidney support. She has coauthored more than 330 published articles and 32 book chapters.

Dr. Ostermann is a senior clinical investigator with a sustained commitment to improving patient outcomes through large-scale research collaboration. She is currently involved in nine active studies within the United Kingdom's National Institute for Health and Care Research portfolio and has completed 43 portfolio studies since 2013. She is a longstanding member of the Acute Disease Quality Initiative group and, since 2016, has served as research faculty for Critical Care Nephrology at the University of Pittsburgh, PA. She also chairs the newly established European Renal Acute Kidney Injury Working Group of the European Renal Association, created in partnership with ASN's AKINow initiative.

Throughout her career, Dr. Ostermann has demonstrated a deep commitment to academic mentorship and clinical education. She holds a postgraduate degree in medical education and was recently appointed director of the Research Leadership Programme at Guy's and St Thomas' NHS Foundation Trust. Dr. Ostermann's academic trajectory spans both basic and translational science: Her PhD from the University of Göttingen, Germany, examined cardiovascular risk in hyperlipidemia, and her MD from the University of London focused on the epidemiology of acute kidney failure in the intensive care unit.

Dr. Ostermann received her medical degree (approbation) in 1990 and earned a PhD in 1991, both from the University of Göttingen. She completed specialist training in intensive care medicine, nephrology, and internal medicine in 2004, with additional clinical training in intensive critical care in Canada and from the European Society of Intensive Care Medicine. She also earned a postgraduate certificate in medical education from the Royal College of Physicians.

Are you a fellow and have a tip or idea you'd like to share with your fellow peers and the broader kidney community?

Send your idea to the ASN *Kidney News* Fellows First column at kidneynews@asn-online.org

PLENARY SESSION

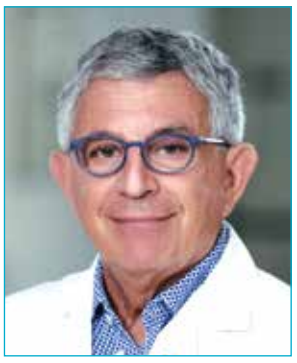
STATE-OF-THE-ART PANEL

State-of-the-Art Panel to Discuss Xenotransplantation Advances

https://doi.org/10.62716/kn.001882025

Xenotransplantation has seen significant advances, driven by the organ shortage crisis and a sustainable alternative to human organ donation. March 2024 marked the first human to receive a genetically modified pig kidney transplant, followed by the first combined heart pump and pig kidney transplant in April 2024. Earlier this year, the US Food and Drug Administration announced clearance of clinical trials for genetically modified pig kidney transplants in humans.

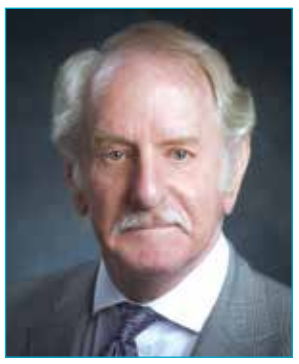
ASN has assembled an expert panel to discuss xenotransplant topics, including surgery and protocols, ethics and selection, translational science, and payment considerations.



Moderator:

Paul E. Klotman, MD
Baylor College of Medicine, Houston, TX

Expert panelists:



David K. C. Cooper, MD, PhD, MA, MS
Massachusetts General Hospital, Harvard Medical School, Boston, MA

Robert A. Montgomery, MD, PhD
New York University, Langone Medical Center, New York City, NY

Leonardo V. Riella, MD, PhD, FASN
Massachusetts General Hospital, Harvard Medical School, Boston, MA

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ASN Comments on Proposed Rule for 2026 ESRD PPS and QIP

By David L. White

https://doi.org/10.62716/kn.002162025

The proposed rule for the 2026 End Stage Renal Disease (ESRD) Prospective Payment System (PPS) and Quality Incentive Program (QIP) (1) raises a great many questions on how the Centers for Medicare & Medicaid Services (CMS) will find improved quality and savings in the future and the end of the ESRD Treatment Choices Model. In a recent letter to CMS Administrator Mehmet Oz, MD, MBA (2), ASN strove to suggest sound policy recommendations to address challenges of the ESRD program and help align the kidney community for future conversations about kidney care that began in earnest during the first Trump Administration.

Financing dialysis

ASN believes that there are inherent challenges with the proposed rule, in which Congress will need to engage with CMS. First, the reliance on the federal government in financing dialysis has grown disproportionately large, especially in the last several years, as commercial insurers pushed their enrollees to shift to Medicare primary coverage. The US Renal Data System reports that since insurers began these practices, the percentage of people relying on commercial coverage between 2012 and 2022 has fallen by more than 36% (3). ASN believes that this downward trend will only continue now that the Supreme Court in *Marietta Memorial Hospital Employee Health Benefit Plan v DaVita Inc*. has reinterpreted the Medicare Secondary Payer Act to allow insurers to eliminate in-network coverage for locally available treatments for kidney failure.

There are several negative consequences to this dynamic, as private insurers are deincentivized to invest in screening and new therapies to slow progression of kidney diseases and prevent kidney failure, knowing that these individuals can be transferred to Medicare's bottom line once they reach kidney failure (at which point, care costs dramatically rise). ASN and the broader kidney community are looking for ways to restore the full power of the Medicare Secondary Payer Act.

Forecast errors

ASN also called on CMS to address the ESRD PPS forecast errors, particularly in capturing the actual costs associated with labor and other factors, leading to potential underfunding for dialysis facilities. These errors arise because the system relies on historical data to forecast annual payment updates. This error can lead to further consolidation of dialysis facilities, which are already condensed to only two companies providing care for more than 80% of all people with kidney failure. These annual forecast errors contribute to a cumulative difference of nearly 7% between the market basket update and actual cost increases since 2019. More than 71% of individuals with kidney failure rely on Medicare for their health insurance coverage. The program is not sustainable for patients unless it is significantly reformed.

Innovation challenges

ASN also focused on innovation challenges in the ESRD program. There is a dearth of research and development for advancing treatments for people living with kidney failure, whereas research and development in other disease states (including earlier stages of chronic kidney disease not reimbursed under ESRD PPS) have seen substantial treatment innovations.

TDAPA eligibility criteria

ASN requested that Transitional Drug Add-on Payment Adjustment (TDAPA) applications be accepted up to 3 years after US Food and Drug Administration (FDA) approval of a new ESRD indication for use as a dialysis drug or biologic product. If a manufacturer obtains FDA approval for a new ESRD indication, then the manufacturer should have 3 years from that new indication to apply for TDAPA. The TDAPA period for new drugs or biologic products inside or outside of an existing functional category should closely mirror the ESRD transition policy applied in the hospital outpatient department and ambulatory surgical centers for price bundling—a period of at least 3 years.

Drug designation process

ASN also requested that CMS take two additional steps:

1. Revise the drug designation process to make sure it is more transparent and involves input from the broader community.
2. Reconsider the use of functional categories to support innovation, and foster competition as intended.

The current CMS process for determining whether a new drug or biologic is designated a renal dialysis service, fits within a functional category, or warrants a new category lacks transparency and meaningful stakeholder engagement. These determinations directly impact patient access and shape

reimbursement pathways, such as TDAPA duration, post-TDAPA adjustments, and whether new funding is integrated into the bundle base rate.

"ASN believes that the reliance on functional categories as a proxy for defining innovation has become a serious barrier to patient access to medically necessary treatments," wrote ASN President Prabir Roy-Chaudhury, MD, PhD, FASN, in the letter to CMS (2). "This construct is not only misaligned with the federal government's own definitions of innovation—such as those outlined by the FDA and HHS [Department of Health and Human Services], which emphasize clinical advancement and addressing unmet medical needs—but it also fails to foster the meaningful competition CMS has identified as a key policy goal."

By equating innovation with functional "newness," the policy creates a structural disincentive for the development of new therapies that may offer substantial clinical benefit but share superficial characteristics with older, less effective treatments. This misalignment has a chilling effect on innovation and represents a missed opportunity to improve patient outcomes. Moreover, the current reimbursement model actively undermines competition.

ASN provided the example of Korsuva (difelikefalin) as the first and only FDA-approved therapy for chronic kidney disease-associated pruritus, a condition affecting approximately 35% of people living with kidney failure. Despite its demonstrated clinical value, Korsuva was placed in a functional category alongside antihistamines like Benadryl (diphenhydramine)—an agent approved in 1946 and widely regarded as ineffective for pruritus. "As a result, no meaningful reimbursement mechanism exists to support Korsuva's continued use. Physicians reported withholding Korsuva prescriptions due to concerns about long-term sustainability, despite recognizing the drug's efficacy and the lack of viable alternatives," Roy-Chaudhury added (2).

Modifications to QIP

ASN expressed disappointment with the removal of health-related social needs measures and offered to work with the administration to identify ways to collect and report this information. ASN also provided direction on:

- modifications to the In-Center Hemodialysis Consumer Assessment of Healthcare Providers and Systems measure
- modifications to QIP

To streamline this effort, ASN recommended that CMS use the following measures in ESRD QIP:

1. standardized hospitalization rate measure (replacing the current ratio measure)
2. standardized readmissions rate measure (replacing the current ratio measure)
3. long-term catheter use
4. patient experience of care: In-Center Hemodialysis Consumer Assessment of Healthcare Providers and Systems survey clinical measure (modified to incorporate the experience of patients on home dialysis as well)
5. serum phosphorus
6. adult hemodialysis Kt/V adequacy measure
7. adult peritoneal dialysis Kt/V adequacy measure
8. pediatric hemodialysis Kt/V adequacy measure
9. pediatric peritoneal dialysis Kt/V adequacy measure
10. percentage of patient-months of pediatric in-center patients on hemodialysis with documented monthly normalized protein catabolic rate measurements
11. clinical depression screening and follow-up measure
12. medication reconciliation reporting measure

Within the Dialysis Facility Compare program, ASN requested that CMS eliminate the following measures:

- Standardized Emergency Department Encounter Ratio for dialysis facilities
- Standardized Ratio of Emergency Department Encounters Occurring Within 30 Days of Hospital Discharge for dialysis facilities
- Standardized Modality Switch Ratio for patients on incident dialysis

ASN expressed its concerns that these measures have validity and reliability problems.

ASN continues to push for statutory changes to address forecast errors, functional categories, TDAPA, and other challenges identified in the letter, especially some of the challenges found in QIP. Other groups are joining ASN's efforts to outline a serious approach to a legislative solution to these issues.

To keep track of ASN's policy efforts to improve the ESRD benefit and its quality outcomes, follow coverage in *Kidney News* and the ASN podcast feed, and visit ASN's Kidney Health Advocacy webpage (https://www.asn-online.org/policy/kidney-health.aspx). For real-time updates from ASN Policy, follow @ASNAdvocacy on X. ■

David L. White is a senior regulatory and quality officer at ASN.

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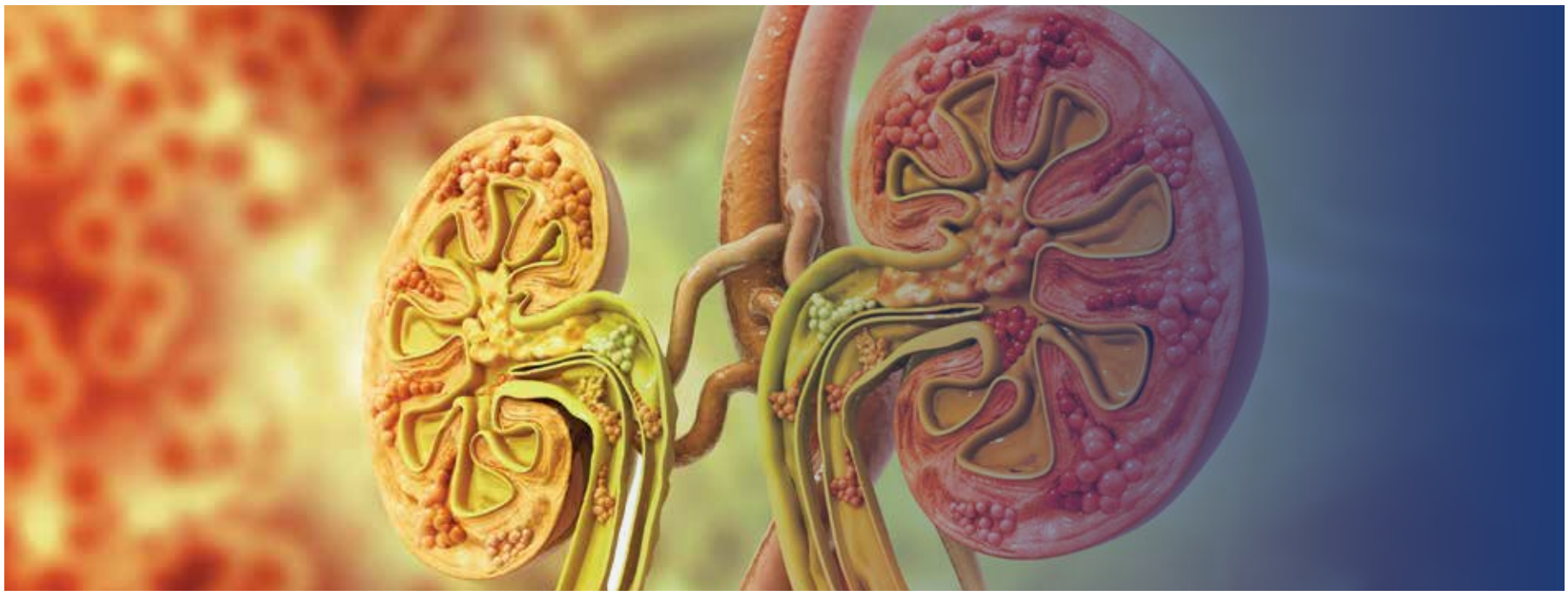


LMD/MS: A More Sensitive Approach to Tissue Diagnosis of PLA2R-Associated Membranous Nephropathy?

By Lois Arend and Tiffany Caza

https://doi.org/10.62716/kn.001422025

Membranous nephropathy (MN) is the second-leading cause of nephrotic syndrome in adults. MN cases are defined by the protein target antigen, of which the most common is phospholipase A2 receptor (PLA2R) (1). Identification of PLA2R positivity in MN has great clinical importance, as serologic testing is available to track anti-PLA2R autoantibodies with disease activity, response to treatment, and disease recurrence.

PLA2R-positive MN represents a renal-limited autoimmune disease, in which a thorough workup for secondary causes may not be necessary. Patients with PLA2R-negative MN require further evaluation to identify an inciting cause and additional typing to identify a target antigen (2). The typical clinical workup for PLA2R-negative MN includes extensive testing to rule out underlying malignancy, autoimmune disorders, sarcoidosis, and infections (3). Multiple antigens have specific clinical associations, which can then guide the clinical workup, and most have evidence of circulating autoantibodies, opening the door for development of serologic assays as available for PLA2R. Currently, over 30 proteins have been identified as targets in MN, and it has become impractical to screen for all of them by standard immunostaining of kidney biopsies. Mass spectrometry (MS) of kidney biopsies following enrichment of glomeruli or recovery of immune complexes provides a means for multiplex testing for all antigens simultaneously and a one-stop test for evaluation of MN cases (4).

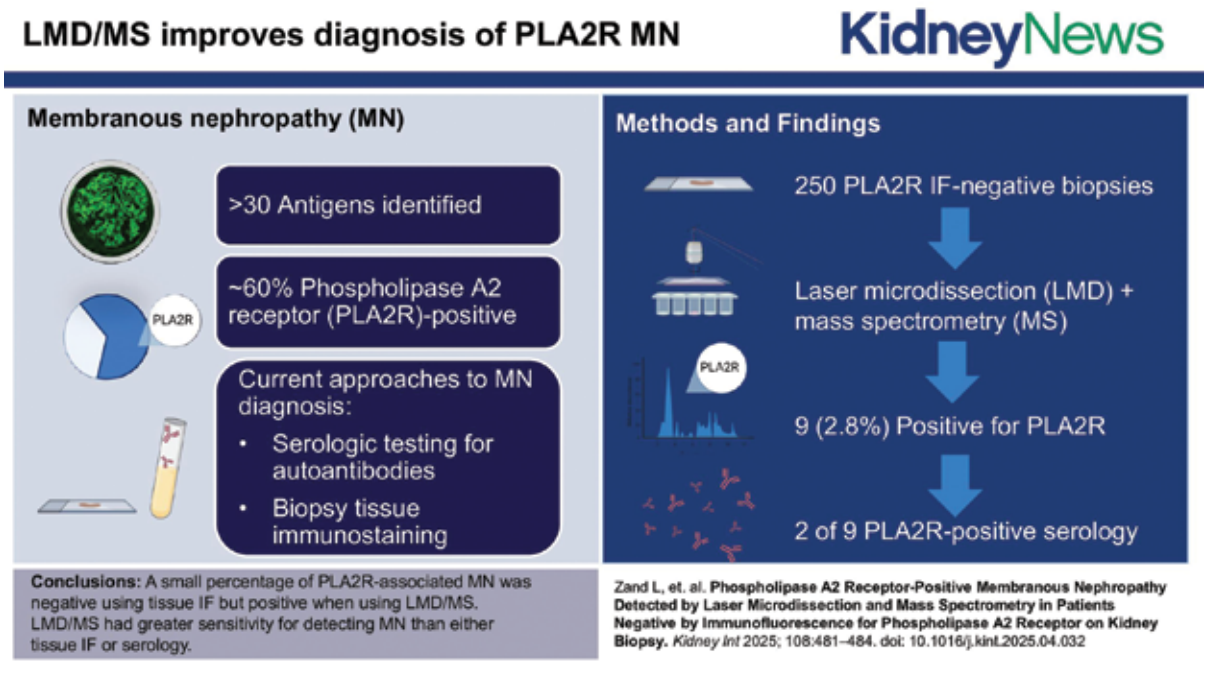
In a recent study at the Mayo Clinic (5), identification of PLA2R by MS was found to have greater sensitivity than through standard immunofluorescence (IF) testing on kidney biopsies. Laser microdissection followed by MS (LMD/MS) was performed in 250 PLA2R-negative MN biopsies, and 9 showed spectral characteristics consistent with PLA2R-associated MN. The cases demonstrated typical findings for MN by light and electron microscopy (EM) and had variable membranous reaction on EM, with Ehrenreich and Churg stages from I to IV, representing a range of chronicity.

Of the nine cases, serologic testing for PLA2R autoantibodies was performed in seven, with two positive for circulating anti-PLA2R antibodies. No correlation was found between spectral counts for PLA2R and PLA2R seroreactivity and titer, intensity of immunoglobulin G (IgG), or stage by EM. Furthermore, the spectral counts in these nine cases were similar to those seen in cases with positive PLA2R staining on IF, indicating no difference in the amount of PLA2R in the tissue.

This study demonstrates improved detection of PLA2R MN by MS over IF of kidney biopsies (5). This has not been the first instance in which MS testing has been found to have increased sensitivity over IF, as it has also been observed with detection of amyloid light-chain amyloidosis (6). Interestingly, patients with MN who are PLA2R seropositive but PLA2R negative were previously reported (7). That study demonstrated that biopsies lacking IF staining on frozen sections showed staining for PLA2R by immunohistochemistry (IHC) on paraffin sections. This suggests that epitope availability is enhanced by the pronase digestion used in the IHC procedure and underscores the importance of knowing the limitations of techniques.

Although the LMD/MS technique avoids the issue of epitope availability entirely, this technique may not be available to many laboratories, whereas IF and IHC are staples of pathologic diagnosis and are used nearly universally. Importantly, Zand and colleagues (5) did not attempt IHC or pronase IF for PLA2R to determine whether the PLA2R antigen could be unmasked in their cohort of cases. If positive using one of these techniques, they could provide a more accessible approach than LMD/MS to cases that are negative on IF but in which the clinical setting would favor a primary form of MN.

The excitement of LMD/MS to characterize many types of kidney diseases has revolutionized the diagnosis of amyloid subtypes and, more recently, antigens responsible for MN. It will be important to view this advancement in the context of the global community and its access to such techniques, however. Given that more than 95% of PLA2R-associated MN can be diagnosed by standard IF or IHC techniques, these remain the gold standard of diagnosis for most laboratories with IF and IHC capabilities. Although MS-based antigen typing for MN is not widely available, identifying the specific autoantigen can reveal the underlying etiology, given established disease associations (2). This knowledge can streamline the diagnostic workup, reducing the need for broad clinical testing, and may uncover reversible disease triggers, potentially slowing disease progression and decreasing long-term health care costs. Eighteen putative MN antigens have been recently identified (8–10), yet their clinical significance



remains unclear due to their rarity but will become evident as more patients are recognized. Serologic assays for newly identified MN antigens are under development and may enable disease monitoring in the future. Consequently, the clinical utility of multiplexed antigen testing is expected to increase over time.

This study underscores the importance of using modern techniques but also demonstrates the limitations of techniques and how their shortcomings can affect clinical care. For example, without the aid of advanced techniques such as LMD/MS, cases of MN that show atypical features on LMD, IF, and EM—such as strong IgA staining, the presence of C1q, nonuniform deposits, or mesangial deposits on EM—could result in incorrect diagnoses, delays in diagnosis, or unnecessary additional testing. In addition, the authors rightly state that as the list of antigens associated with MN continues to grow, performing IF/IHC for all antigens may become untenable. As other conditions have shown us, advanced techniques may replace the gold standards of IF and EM; diagnosis of diseases such as Alport syndrome, Fabry, and others now relies heavily on genetic testing rather than histologic procedures.

Whether MS is used in the clinical workflow or evaluation of MN cases, it is important to recognize that PLA2R-positive MN cases may have false-negative staining on biopsies (5, 7). In lieu of MS, serologic testing for PLA2R may be considered for exclusion of this most common form of MN. It is unknown whether this phenomenon of increased sensitivity by MS is unique to PLA2R, and further work may also identify whether MS demonstrates greater sensitivity for detection of other antigens in MN. ■

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The authors report no conflicts of interest.

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INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

TAVNEOS (avacopan) 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

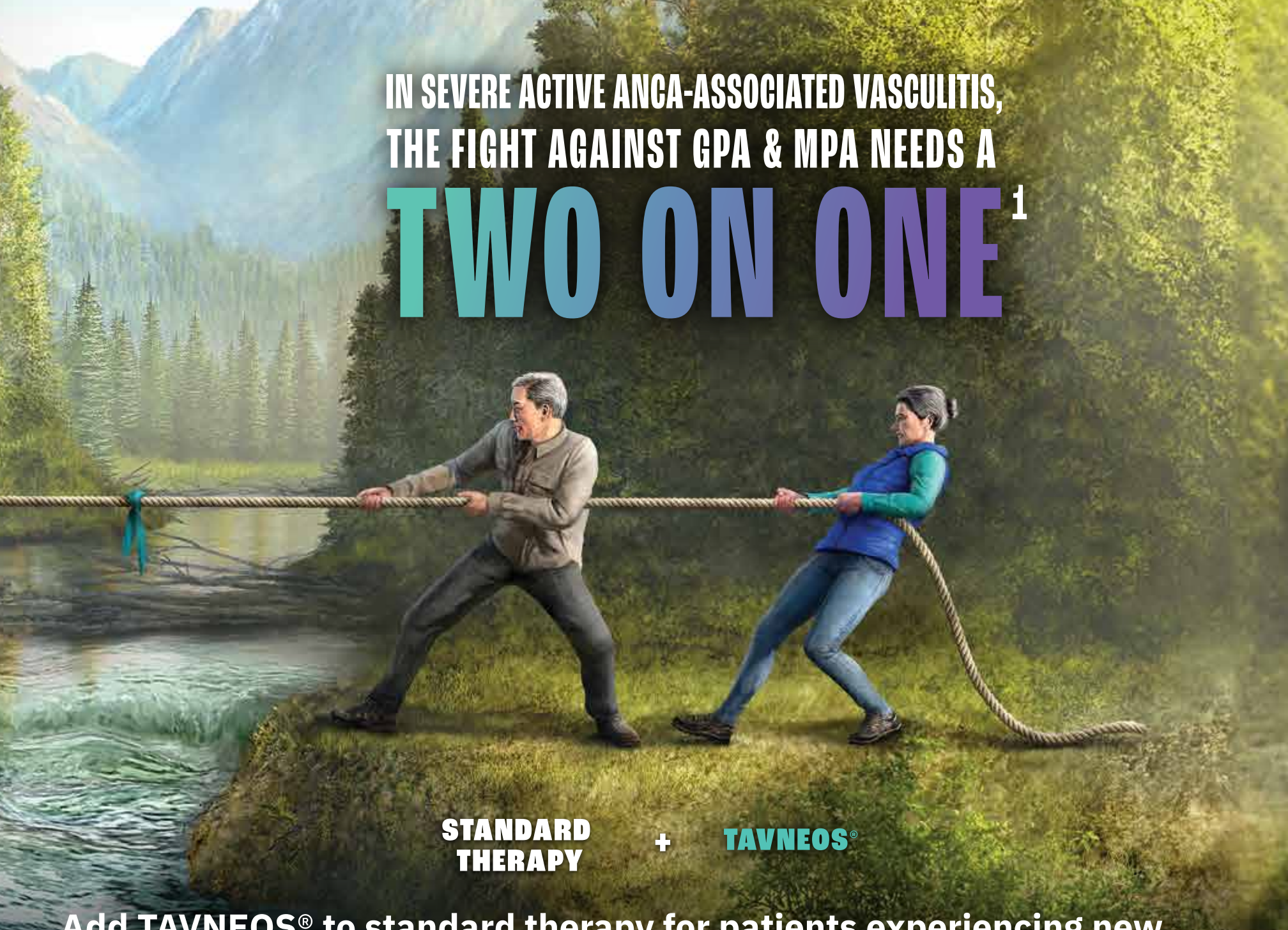
Serious hypersensitivity to avacopan or to any of the excipients.

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.



Add TAVNEOS® to standard therapy for patients experiencing new, relapsing, or persistent disease activity[1,2]

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 co-administration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when co-administered with strong CYP3A4 enzyme inhibitors to 30 mg once daily. Consider dose reduction of CYP3A4 substrates when co-administering TAVNEOS. Co-administration of avacopan and 40 mg simvastatin increases the systemic exposure of simvastatin. While taking TAVNEOS, limit simvastatin dosage to 10 mg daily (or 20 mg daily for patients who have previously tolerated simvastatin 80 mg daily for at least one year without evidence of muscle toxicity). Consult the concomitant CYP3A4 substrate product information when considering administration of such products together with TAVNEOS.

TAVNEOS is available as a 10 mg capsule.

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 [package insert]. Cincinnati, OH: Amgen Inc. **2.** Chung SA, Langford CA, Maz M, et al. *Arthritis Rheumatol*. 2021;73(8):1366-1383.

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

05/25 USA-569-81131

AMGEN

BRIEF SUMMARY OF PRESCRIBING INFORMATION
TAVNEOS® (avacopan) capsules, for oral use
Please see package insert for full Prescribing Information.

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.

CONTRAINDICATIONS

TAVNEOS is contraindicated in patients with serious hypersensitivity reactions to avacopan or to any of the excipients *[see Warnings and Precautions (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 (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 (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 TAVNEOS to a patient with liver disease. Monitor patients closely for hepatic adverse reactions *[see Use in Specific Populations (8.7)]*.

Hypersensitivity Reactions

TAVNEOS may cause angioedema *[see Adverse Reactions (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 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 (5.1)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.2)]*
- Hepatitis B Virus (HBV) Reactivation *[see Warnings and Precautions (5.3)]*
- Serious Infections *[see Warnings and Precautions (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 (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 (12.3)]*. Avoid co-administration 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 (12.3)]*. Administer TAVNEOS 30 mg once daily when co-administered with strong CYP3A4 inhibitors.

CYP3A4 Substrates

Avacopan is a moderate CYP3A4 inhibitor. Co-administration of avacopan and 40 mg simvastatin increases the systemic exposure of simvastatin. While taking TAVNEOS, limit simvastatin dosage to 10 mg daily (or 20 mg daily for patients who have previously tolerated simvastatin 80 mg daily for at least one year without evidence of muscle toxicity). Consider dose reduction of CYP3A4 substrates when co-administering TAVNEOS with CYP3A4 substrates. Consult the concomitant CYP3A4 substrate product information when considering administration of such products together with TAVNEOS *[see Clinical Pharmacology (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 Toxicology (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 (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 (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 (12.3)]*. TAVNEOS has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www.tavneospro.com or contact Amgen Medical Information at 1-800-772-6436.

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TAVNEOS® (avacopan)

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PRACTICE RESOURCE

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ASN American Society of Nephrology | JASN Journal of the American Society of Nephrology

Using Extrapolation to Accelerate Clinical Trials in Pediatric Nephrology

By Howard Trachtman and Cesia Creighton

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Chronic kidney disease (CKD) is fortunately a rare clinical entity in children and adolescents. In addition, the causes of CKD in the pediatric population are different than those in adults; congenital anomalies of the kidney and urinary tract account for up to half of the youths who progress to kidney failure during childhood. Coupled with the important legal and ethical constraints on the conduct of clinical research in young patients, these two factors have hampered the conduct of randomized controlled trials (RCTs) in pediatric nephrology. As a consequence, there is a 13-year gap between the approval of new drugs for use in adults and subsequent approval in children (1). In that time interval, pediatric nephrologists are forced to resort to off-label use of new therapies without adequate dosing guidelines for smaller patients and to use only adult-derived safety information. This problem was highlighted in a workshop jointly organized by the Kidney Health Initiative (KHI), a partnership between ASN and the US Food and Drug Administration, and NephCure in July 2023 that addressed the need to assess the efficacy and safety of sodium-glucose cotransporter-2 inhibitors in children and adolescents with CKD.

To overcome this hurdle and enhance the feasibility of conducting RCTs in pediatric nephrology, regulatory authorities have recommended the use of extrapolation of CKD data from adults to children as a tool to facilitate the implementation of clinical trials in a full range of pediatric kidney diseases associated with development of CKD. Briefly, extrapolation posits that if a kidney disease has a similar natural history, response to therapy, and clinical outcome in children and adults, then it is justified to extrapolate the efficacy findings in adults with the disease to the parallel population in pediatrics and in this way, potentially limit the scope of an RCT. The degree of similarity between children and adults with a kidney disease will vary along a spectrum, and the extent of extrapolation should vary accordingly. An initiative called POLARIS (Extrapolation to Support Clinical Trials in Pediatrics) was organized to promote the implementation of extrapolation in the design of RCTs in pediatric nephrology. It is centered on three key areas of interest: optimizing clinical data, development of biomarkers, and risk prediction tools.

Bridging the gap

To promote awareness of the potential use of extrapolation, KHI and the International Society of Glomerular Disease (ISGD) sponsored a workshop entitled, "Bridging the Gap: Advancing Pediatric Kidney Care Through Data Extrapolation," on May 21, 2025, as part of KHI's annual meeting in Washington, DC. The workshop was organized by Louise Oni, MBChB, MRCPCH, MA, PhD (University College London, UK); William E. Smoyer, MD (Nationwide Children's Hospital, Columbus, OH); and article coauthor Howard Trachtman, MD, FASN (University of Michigan, Ann Arbor). "This workshop was designed to be a logical extension regarding the most appropriate clinical settings for the use of pediatric extrapolation that was discussed at the 2023 multi-stakeholder workshop on sodium-glucose cotransporter-2 inhibitor use in children with CKD," said Smoyer. The workshop was fully preregistered, and 50 people, including clinical nephrologists, industry partners, regulatory officials, and patient advocates, contributed to the proceedings.

After an opening presentation by Oni that put the current status of clinical research and drug development in pediatric nephrology in perspective, Kirtida Mistry, MBBCh, DCH, MRCPCH, FASN (Division of Cardiology and Nephrology, US Food and Drug Administration, Silver Spring, MD), introduced the workshop with an overview of extrapolation and how regulatory authorities envision its role in RCT design. Petter Bjornstad, MD (University of Washington, Seattle), provided a summary of traditional and novel biomarkers that may be used in assessing outcomes. He highlighted the potential utility of bridging biomarkers as the primary endpoint in RCTs for pediatric CKD by predicting the degree of change in response to treatment, as many biomarkers have been shown to be highly associated with the change in the clinical outcome. In the third portion of the workshop, Michelle Denburg, MD, MSCE (Children's Hospital of Philadelphia, PA), presented updates from the ESCAPE (Effect of Strict Blood Pressure Control and ACE-Inhibition on Progression of Chronic Renal Failure in Pediatric Patients) (2) and Chronic Kidney Disease in Children (3) cohorts and the PEDSnet consortium (4), which documented the importance of blood pressure, proteinuria, and other novel mediators that can identify children and adolescents at increased risk of disease progression regardless of the underlying cause. Finally, a panel of industry participants, Julie Lin, MD, FASN, MPH (Travere Therapeutics, San Diego, CA); Marvin V. Sinsakul, MD, MBA (AstraZeneca, Gaithersburg, MD); and Jennifer McKenzie, MD (Boehringer-Ingelheim, Ridgefield, CT), provided the perspective of industry sponsors about the application of extrapolation. All four components of the program promoted lively and insightful interaction with members of the audience.

Overall, the workshop successfully highlighted the potential of extrapolation to facilitate RCTs in pediatric nephrology. Mark D. Lim, PhD, ASN Vice President of Research, Discovery, and Innovation and strategic lead for KHI, said, "The Kidney Health Initiative's Board of Directors continues to prioritize pediatric clinical trials. POLARIS presents an approach that could simplify the conduct of these clinical trials for many kidney diseases." The consensus of all participants was that this is an important initiative that has the potential to substantially change the landscape for clinical trialists and industry partners who seek to evaluate the efficacy and safety of novel therapies in children among the full range of kidney diseases.

A united goal

The open discussion at the KHI/ISGD workshop indicates that there is much work that needs to be done to make extrapolation a viable part of pediatric RCT design and implementation. However, the energy and enthusiasm displayed at the workshop indicated a genuine commitment among all of the key sectors to "roll up their sleeves" and make extrapolation happen through the POLARIS initiative. This will be to the benefit for youths with kidney diseases, their families, and all of those who care for them.

Putting the workshop in a larger perspective, Oni commented, "This popular event marked an important milestone for children with kidney diseases, and I am grateful to KHI and ISGD for bringing together exceptional attendees. The rich information gained from the participants will be used to inform a highly collaborative program to develop guidance on how data extrapolation can advance our specialty as we work toward a united goal to reduce kidney failure in childhood." ■

Howard Trachtman, MD, FASN, is with the University of Michigan Medical School, Ann Arbor, and served as co-organizer of the May 2025 workshop discussed in this article. Cesia Creighton, MPH, is the Kidney Health Initiative Senior Program Coordinator, Washington, DC.

The authors report no conflicts of interest.

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Fostering Innovative Leaders in Nephrology and Dialysis (FIND): Growing Future Generations of Leaders

By Cynthia Delgado, Joseph Kessler, Liz McNamara, and Christina Silva on behalf of the FIND Steering Committee

https://doi.org/10.62716/kn.001692025

In January 2025, ASN launched the Fostering Innovative Leaders in Nephrology and Dialysis (FIND) program to empower future generations of leaders who will drive innovation, advance clinical care, and champion positive policy change for people living with kidney diseases. FIND welcomed an inaugural cohort of 11 early-career nephrology professionals from across the United States to participate in this comprehensive 12-month program.

FIND aligns with ASN's broader goals to accelerate innovation and enhance patient-centered care. ASN's diverse membership, now exceeding 21,000, includes professionals from academia, clinical practice, research, policy, pharmacy, and interventional nephrology. FIND is leveraging this membership to mentor and train participants with critical leadership competencies needed to address challenges within nephrology and dialysis care.

There is a documented skills gap in nephrology leadership training. Leadership skills are increasingly recognized as crucial for medical professionals to navigate the complexities of health care and improve patient outcomes. Yet, to date, traditional medical training lacks leadership training, leaving professionals without the needed skill set to address real-world challenges (1). Formal leadership curricula elevate professional confidence and enhance capabilities, underscoring the importance of the FIND training program. FIND participants engage in personalized mentorship, interactive roundtable discussions, independent self-paced leadership education modules, and a leadership capstone project addressing real-world issues in nephrology. The inaugural class individually developed capstone projects covering several key thematic areas including quality improvement, patient engagement, health equity, workforce development, and health policy.

Acquiring leadership skills at the beginning of a professional career is challenging and is often ignored in favor of focusing on job skills training. As health care continues to evolve, nephrology professionals must be prepared with essential leadership skills and knowledge to navigate future opportunities and challenges. Moving away from the "on the job training" model for leadership, in which only one method of leadership may be taught, is critical to growing future generations of nephrology leaders (2). FIND introduces mentees to a variety of leadership styles through interaction with prominent leaders in the field of nephrology. In addition to working with a leadership mentor, FIND also fosters networking opportunities through roundtable discussions and in-person events. Following program completion, alumni will have ongoing opportunities to network and collaborate with future FIND cohorts and ASN leaders, fostering continuous leadership growth and contributions to nephrology.

2025 FIND curriculum overview

- Program Introduction, Bias Training, Capstone Project Overview
- Strength & Leadership Assessments Reflection
- Roundtable: Leading Change
- Emerging Leaders Panel: Personal Leadership Journeys
- Capstone Project Outline Presentations
- Interdisciplinary Roundtable: Team-Building Strategies
- Policy & Regulation Impact on Health Care
- Crisis Leadership, Emotional Intelligence, & Essential Leadership Skills
- Capstone Project Final Presentation (in-person)
- Interactive Leadership and Conflict Management (in-person)
- ASN Initiatives and Opportunities

For further details about FIND, please visit the website by scanning the QR code. ■

bit.ly/46tDt7x

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KidneyCure: A Commitment to Supporting the Future of Nephrology

By Deidra C. Crews, Jeffrey H. Miner, and Lynee Galley

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The future of kidney research and care depends on commitment to both scientific discovery and the development of the nephrology workforce. For more than 3 decades, ASN and its philanthropic foundation, KidneyCure, have contributed to the growth of the kidney research community through grants and fellowships, shaping today's as well as the next generation's leaders of the field. KidneyCure offers kidney researchers and faculty a pathway to developing a career focused on advancing nephrology research.

Supporting tomorrow's kidney researchers today

Founded in 2012 as the ASN Foundation for Kidney Research, KidneyCure has awarded over $50 million, making it the largest private funder of kidney-focused research. By distributing more than $3 million annually to early-career research investigators in both basic and clinical research, KidneyCure supplements research and fellowship funding offered by the federal government and other private funders to sustain progress in kidney research. KidneyCure provides competitive fellowships and grants across these early-career stages to increase the kidney research workforce.

KidneyCure Pre-Doctoral Fellowship

Launched in 2018, this fellowship supports graduate-level PhD candidates conducting kidney research under the mentorship of a senior kidney-focused investigator. According to Kurt Amsler, PhD, associate dean of research at the New York Institute of Technology College of Osteopathic Medicine and former cochair of the Pre-Doctoral Fellowship Review Panel, the program has helped retain emerging scientists in the field and has fostered the application of innovative research techniques to key questions in nephrology.

Ben J. Lipps Research Fellowship

This program supports postdoctoral fellows committed to advancing nephrology through mentored research. Since its inception, more than 100 fellows have received support through this program, leading to high-impact peer-reviewed publications, faculty appointments, and additional kidney-focused grant funding. According to author Jeffrey H. Miner, PhD, FASN, who serves as ASN Council's Liaison to ASN's Grant Review Committee, "The fellowships not only help draw in young investigators and keep them in our field but also support mentors' laboratories and encourage the development of outstanding mentoring skills."

Transition to independence grants

Designed to help early-career faculty establish independent research careers, this program aims to equip recipients to be competitive for an R01 grant from the National Institutes of Health (or an equivalent award) by the end of the KidneyCure award period. Securing federal and nonfederal research funding has become increasingly competitive—in 2024, the success rate for new R01-equivalent submissions declined by 2.9%, reaching just 19% (1). As KidneyCure's longest-running program, this support has advanced the careers of more than 200 investigators, with two-thirds successfully obtaining R01 funding to date. As highlighted by author Deidra C. Crews, MD, ScM, FASN; ASN past president; and chair of the

KidneyCure Board of Directors, "KidneyCure's support for promising early-career investigators is essential during this time of uncertain federal support for biomedical research."

KidneyCure recently updated the eligibility criteria for this program for the upcoming grant cycle. An applicant must now be within 12 years of receiving a clinical terminal degree (excluding residency and clinical fellowship training years) or within 10 years of receiving a PhD or MD/PhD (also excluding clinical fellowship training years for the latter).

William and Sandra Bennett Clinical Scholars Program

The Bennett Clinical Scholars Program reinforces ASN's commitment to excellence in nephrology education and teaching. This program supports the career development of nephrology educators by funding initiatives focused on curriculum design, clinical instruction, and educational innovation.

Looking ahead: Apply by November 20, 2025

KidneyCure is now accepting applications for the 2026 grant cycle. Faculty, mentors, training directors, and other leaders are encouraged to inform their nephrology trainees, predoctoral students, fellows, and early-career faculty about this funding opportunity. Eligible individuals are also invited to explore available grant opportunities for themselves. KidneyCure aims to strengthen a pipeline of innovation and research leadership, bringing us closer to a world without kidney diseases.

For full details on eligibility, programs, and application guidelines and to apply for a KidneyCure grant, please visit www.kidneycure.org. ■

Deidra C. Crews, MD, ScM, FASN, is professor of medicine at Johns Hopkins University School of Medicine, deputy director of the Johns Hopkins Center for Health Equity, Baltimore, MD. Jeffrey H. Miner, PhD, FASN, is the Eduardo and Judith Slatopolsky Endowed Professor of Medicine in Nephrology and the director of Basic Research in the Division of Nephrology at Washington University School of Medicine, St. Louis, MO. Drs. Crews and Miner serve on the KidneyCure Board of Directors. Lynee Galley is director, Research, Discovery, and Innovation at ASN.

The authors report no conflicts of interest.

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Glomerular Diseases Collaborative: Improving Outcomes Through Connection and Bridging Knowledge Gaps

By Keisha Gibson and Christina Silva on behalf of the Glomerular Diseases Collaborative Steering Committee

https://doi.org/10.62716/kn.001702025

The Glomerular Diseases Collaborative (GD-C), launched in 2024, aims to promote high-quality care for people living with GD and to stimulate opportunities to address gaps in knowledge, training, continuing education, and awareness across the spectrum of GD.

Led by Keisha Gibson, MD, MPH, FASN, GD-C is comprised of a diverse group that includes a patient advocate and clinical GD experts. Alan Kliger, MD, chair of the ASN Excellence in Patient Care Advisory Committee and ad hoc member of GD-C, emphasized the significance of this initiative: "I think that this is one of the most important things that ASN is doing. And the reason is that we are really at an inflection point. I've been a nephrologist now for over 50 years, and in that time, it's only within the last few years that we actually have had specific medicines and specific treatments for glomerular diseases. And it's really the beginning of a whole change in the way we're looking at chronic disease."

Powered by partnership: GD-C industry roundtable

Recognizing the importance of improving access to treatment for GD, GD-C held a roundtable on May 25, 2025, that included several pharmaceutical industry representatives and clinicians with expertise in GD. The mission was to foster open dialogue, share knowledge, and develop strategies to amplify existing resources and break down barriers to access treatment for GD.

Patrick Nachman, MD, FASN, GD-C Steering Committee member, reflected on the event's impact: "I think it [GD-C] brings together a group of folks, patients, academicians, pharma, in the same venue, in the same group, thinking together about what [the obstacles are] that we could address. How can we not only develop new drugs but [also] think about how we can make these new therapies accessible to the patients who need them, no matter where they are in the world?"

Key roundtable themes included:

- early disease identification and outreach
- drug access and systemic barriers
- communication and promotion strategies
- metrics, evaluation, and value

GD Compendium: A living resource

Designed for busy community nephrology and primary care professionals, the GD Compendium is a collection of online resources from a variety of outstanding GD organizations offering streamlined access to clinical guidelines, up-to-date content on GD, drug-specific treatment, and links to patient educational materials. Developed by working groups of clinical GD experts and patient advocates nationwide, the compendium ensures practical, up-to-date content.

The GD Compendium is meant to showcase the dedication and ongoing efforts being done to support health care professionals and patients. It will serve as a living resource to keep up with the ever-changing and exciting landscape of GD.

Current chapters include:

- GD Overview
- Navigating Access to Treatment
- ANCA-Associated Vasculitis
- IgA Nephropathy
- Lupus Nephritis
- C3 Glomerulopathy
- Membranous Nephropathy

Luis Sanchez Russo, MD, MS, community nephrologist and working group member, added: "Who can benefit from the GD Compendium? Ultimately, everybody. But above all, the patients. I think that we drive for the patients, and I think that narrowing the gap between research and finally, the application in the field [are] going to be very beneficial for the patients."

New *JASN* publication

A perspective piece, "Barriers to Patients Accessing Specialized Treatments for Glomerular Diseases," was authored by several members of the GD-C Steering Committee and published in *JASN* this past summer (1). It highlights critical barriers, including limited access to specialists, administrative hurdles that impede patients with GD from receiving timely treatment, and calls for policy and system reforms to improve care delivery.

For access to the GD Compendium, continued updates, expanded chapters, and more ways in which the GD-C is transforming GD care, please visit the website by scanning the QR code. ■

Keisha Gibson, MD, MPH, FASN, is chair of the Glomerular Diseases Collaborative (GD-C) Steering Committee and a nephrologist at the University of North Carolina Kidney Center, Chapel Hill. Christina Silva, BSN, RN, is a clinical project specialist at ASN and staff lead for GD-C.

The authors report no conflicts of interest.

Support for GD-C is provided by Alexion Pharmaceuticals, Inc.; Calliditas Therapeutics; Novartis Pharmaceuticals Corporation; Otsuka; Travere Therapeutics, Inc.; Vera Therapeutics; and Vertex Pharmaceuticals.

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Humanitarian Kidney Support Program: Responding to Evolving Needs

By Jeffrey Silberzweig and Liz McNamara on behalf of the HKSP Steering Committee

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ASN's Humanitarian Kidney Support Program (HKSP) is a coalition dedicated to supporting people with kidney diseases and kidney health professionals in: natural and man-made disaster preparedness and response; identification of current and emerging threats; and development and support of a sustainable dialysis system with a strategic focus on climate impact. Its mission is to set the direction for ASN's efforts to provide humanitarian support for kidney communities in North America and the Caribbean affected by disasters, biologic threats, and climate- and heat-related injury through collaboration, education, and advocacy.

HKSP has three components: emergency preparedness and response, sustainability, and current and emerging threats (CET).

Emergency preparedness and response

After Hurricanes Irma and Maria in September 2017, ASN provided logistical support to kidney care professionals and people living with kidney diseases. Collaborating with dialysis and relief organizations, ASN helped to (1) inform the kidney community about the extent of each emergency and (2) identify open dialysis centers. Recognizing the certainty of future disasters, ASN formed the Emergency Partnership Initiative, which evolved into the Emergency Preparedness and Response (EPR) Committee.

In 2024, Hurricane Helene caused extensive damage to a Baxter health care manufacturing plant, which provides most of the peritoneal dialysis fluid used in the United States. EPR collaborated with the ASN policy team and ASN leadership to author guidance for the preservation of peritoneal dialysis fluids while avoiding negative impact on patient care and outcomes.

Recent EPR efforts have focused on helping the kidney community prepare for emergencies. EPR has released a learning module, "Emergency Preparedness for Dialysis Providers and People Living With Kidney Diseases," to educate nephrology professionals on general emergency preparedness, the importance of facility response plans, and guidance for specific events.

Sustainability

Dialysis care has a large environmental impact, including water consumption (>450 billion L annually), energy consumption, greenhouse gas emissions, and massive generation of waste, such as plastics like dialyzers and bloodlines (3–9).

The Sustainability Committee will define ASN's focus on sustainable nephrology practice and build on both national and international partnerships. For example, ASN has representatives on the International Society of Nephrology's Global Environmental Evolution in Nephrology and Kidney Care (Green-K) Steering Committee, with a mission of sustainable kidney care for a healthy planet and healthy kidneys (10), and the Kidney Diseases: Improving Global Outcomes (KDIGO) Controversies Conference on Green Dialysis.

ASN's Sustainability Committee is currently defining action items that will include efforts to educate and support green nephrology care.

CET

The mission of CET is to enhance the quality of life for people with kidney failure by engaging nephrologists as team leaders in transformational change that continuously improves the safety of life-sustaining dialysis, specifically in the areas of current and emerging bacterial, viral, and fungal threats that impact individuals living with kidney diseases.

Recent CET efforts include the Multidrug Resistant Organisms Compendium, which is designed to help heath care professionals better understand risks, testing, infection prevention and control precautions, and treatments for multidrug resistant organisms. The first sections include an introduction, general infection prevention and control recommendations, and *Candida auris*. The compendium will continue to grow as antimicrobial-resistant organisms become greater safety concerns to patients in the nephrology population. Additionally, CET released frequently asked questions for avian influenza and measles in response to current threats.

Providing quality care to individuals with kidney diseases requires adapting to changing circumstances. ASN's HKSP, through its EPR, Current and Emerging Threats, and Sustainability Committees, is well-positioned to help the kidney community respond to evolving world conditions, now and into the future.

For further details about HKSP, please visit the website by scanning the QR code. ■

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Jeffrey Silberzweig, MD, FASN, is the chief medical officer of the Rogosin Institute and professor of clinical medicine and clinical medicine in surgery, Weill Cornell Medical College, New York, NY. Dr. Silberzweig is also chair of HKSP and cochair of ASN's Current and Emerging Threats Workgroup. Liz McNamara, MS, RN, is the ASN staff liaison to HKSP and a member of the ASN Excellence in Patient Care team.

The authors report no conflicts of interest.

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Saving Kidneys, Hearts, and Lives: Call to Action for the Nephrology Community

By Alan S. Kliger and Melissa West

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An artificial kidney to treat kidney failure was the dream of the early 20th century. During World War II, Willem Kolff hid several prototype new machines called hemodialyzers from the Nazis. This machine and others like it produced a revolution for people with progressive kidney diseases, allowing individuals with terminal kidney failure to survive, thrive, and receive kidney transplants. A multibillion-dollar industry grew to support the lives of over 2 million people worldwide with kidney failure. Over the years, this early revolutionary approach stabilized, as nephrology focused largely on describing the pathophysiology of various kidney diseases and using kidney replacement therapies, dialysis, and kidney transplant for people with kidney failure.

The real prize—maintaining kidney function and preventing kidney failure—awaited development of new therapies in the 21st century. When the cellular pathways of several glomerular diseases were uncovered, medications were developed to alter their pathophysiology, and people with these disorders began to benefit. The larger group of individuals experiencing other causes of kidney failure had only kidney replacement to look forward to until studies showed that angiotensin-converting enzyme inhibitors (ACEis) and angiotensin II receptor blockers (ARBs) had a modest effect on reducing the progression of kidney failure. At the beginning of the 21st century, the best care for people with progressive kidney diseases was management of comorbidities like diabetes and hypertension, bicarbonate for some, and ACEis or ARBs, particularly for those with proteinuria and some glomerular diseases.

The big opportunity to prevent kidney failure and maintain kidney function really came as a surprise. Several drugs initially designed to treat diabetes were shown to have a surprisingly strong effect on preserving kidney function and are described as follows.

1. Sodium-glucose cotransporter-2 inhibitors, which inhibit glucose reabsorption in the proximal tubule, were used to reduce blood glucose in patients with diabetes by increasing glucose excretion. While they proved to be relatively poor anti-diabetes drugs compared with others, they had marked benefits on kidney function (1), stopping or slowing loss of kidney function, and preserving kidneys. They also had a beneficial effect on the heart in patients with congestive heart failure.
2. A second class of medication, glucagon-like peptide-1 receptor agonists, stimulates insulin release, suppresses the release of glucagon, slows gastric emptying, and increases satiety. An effective diabetes treatment, these agents also lead to weight loss. These medications also were found to reduce proteinuria and to slow progression of kidney diseases (2).
3. Mineralocorticoid receptor antagonists block the effects of aldosterone and reduce blood pressure and intravascular volume. Studies of nonsteroidal mineralocorticoid receptor antagonists show that they also reduce proteinuria and slow progression of kidney diseases (3).

A new paradigm

Studies now underway, or recently published, suggest that for some patients, the effectiveness of these medications may be additive to protect the kidney. Now, for the first time, to our knowledge, these drugs used alone or in combination appear to protect the kidney, prevent or ameliorate deterioration of kidney function, and at the same time, protect the heart and prevent congestive heart failure. This offers a new paradigm for nephrology: saving kidneys, hearts, and lives.

The nephrology community's challenge is how to accelerate adoption of these life-saving treatments. Translation of science to the bedside has sometimes been painfully long; for example, it took 17 years on average for the majority of eligible people with kidney diseases to receive ACEis or ARBs after they were shown to be effective. What can be done to ensure that eligible patients receive these new treatments to protect their kidneys and hearts now?

ASN is rolling out a vigorous campaign to save kidneys, hearts, and lives now. This multidisciplinary effort will provide the necessary education and information to community nephrologists and the care team, as well as assist health systems and academic centers with implementation of new models of care. Working together, the community will help define how nephrologists amplify the message that now is the time to intervene earlier to protect kidney function and define the collaboration with primary care, endocrinology, cardiology, and sister specialties to advance kidney care.

The kidney world is not alone in recognizing the importance of these new treatments. The world of heart disease has moved rapidly in its translation work, bringing the science to the patient, with guideline development and community outreach underway. The work of the American Heart Association (AHA) is led through its presidential advisory and 4-year commitment called Cardiovascular, Kidney, and Metabolic Health. AHA has defined 15 markets in which its campaign will reach 265,000 people in 4 years. Although AHA's work does include some attention to the kidney, ASN is planning a parallel and collaborative campaign to focus more directly on people with kidney diseases, leveraging work already accomplished and championing partnership to drive a common goal: assuring drug availability and knowledge to all clinicians and people with kidney diseases.

First steps

ASN will engage with AHA, the American Kidney Fund, the National Kidney Foundation, and others to drive awareness, disseminate educational materials, and support outreach. Through this broader learning collaborative, lessons learned will influence future designs. ASN is also developing Kidney Health Guidance to leverage and supplement forthcoming American College of Cardiology/AHA guidelines in development, specifically focused on the kidney disease community. Finally, ASN is developing pathways to engage ASN members now to promote the best ways to save kidneys, hearts, and lives, which is its 21st century pledge to stop kidney diseases and preserve kidney function. ■

Alan S. Kliger, MD, is a clinical professor of medicine, Yale University School of Medicine, and chair of the ASN Excellence in Patient Care (EPC) Advisory Committee. Saving Kidneys, Hearts, and Lives is a program within EPC. Melissa West is senior director, Strategic Relations and Patient Engagement, at ASN.

The authors report no conflicts of interest.

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ASN's Centers of Excellence Initiative: Advancing Home Dialysis Care

By Edward Gould and Kerry Leigh on behalf of the
ASN Centers of Excellence in Home Dialysis Task Force

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In recent years, a renewed focus has emerged on enhancing patient access to home dialysis therapies as well as on ensuring high-quality care delivery for patients choosing home dialysis as a primary modality for kidney failure care. This focus aligns with the objectives of the Advancing American Kidney Health Executive Order of 2019 (1), which charged the nephrology community with improving kidney health outcomes. Concurrently, there is increased interest in promoting patient-centered care by recognizing that dialysis options are aligned with individual patient needs, circumstances, and preferences.

Although ASN has long championed home dialysis support through direct policy and advocacy work, as well as by commenting on regulatory initiatives through the ASN Quality Committee, there is recognition that additional opportunities may be leveraged. To help the nephrology community meet this charge, ASN launched the Centers of Excellence in Home Dialysis Task Force in the spring of 2025. The task force aims to understand exactly what "centers of excellence" means in this space and to then craft a pilot program that could aid nephrology clinicians as they seek to build, grow, and manage home dialysis programs in an increasingly complex medical landscape. To date, the task force has conducted both virtual and in-person meetings, engaging in extensive discussions regarding potential opportunities and challenges inherent in establishing a Centers of Excellence in Home Dialysis program. Following an in-person gathering, several foundational concepts relevant to promoting patient centeredness and high-quality care for home dialysis in the United States were identified.

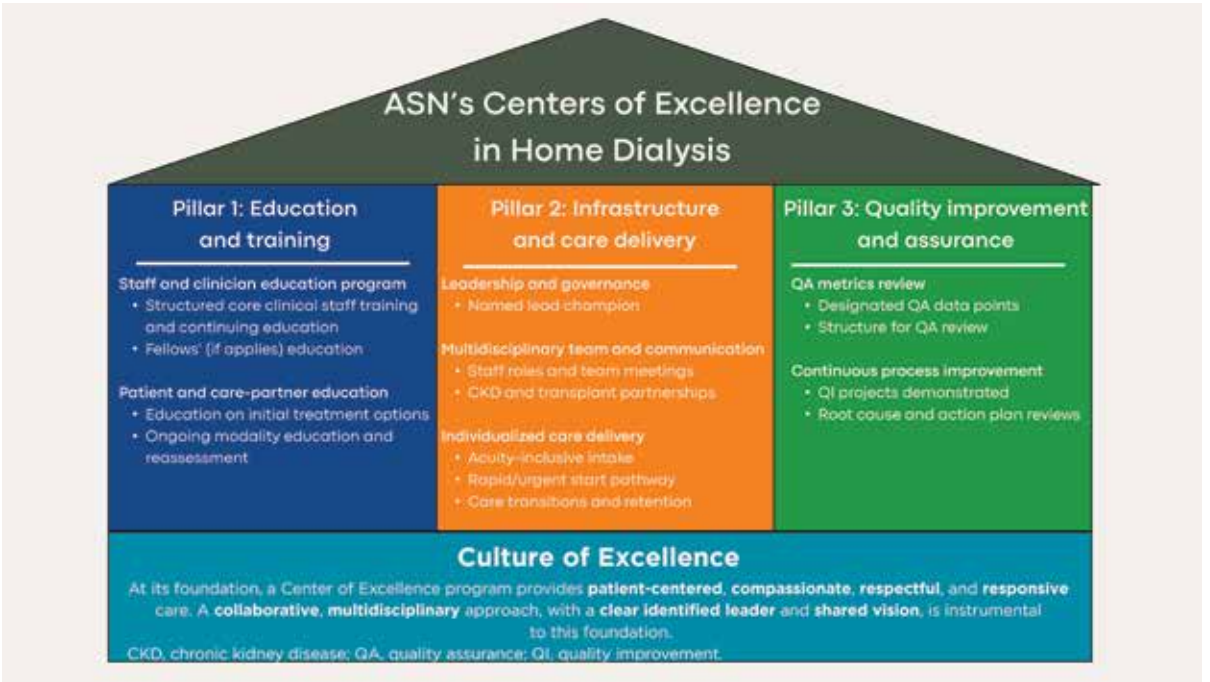
Core principles and pillars of excellence

A fundamental finding from the task force discussions is that effective home dialysis care is predicated on a program culture that fosters collaborative interactions among the interdisciplinary care team. This concept was universally acknowledged as critical for promoting favorable patient outcomes, enhancing workforce satisfaction, and stimulating innovative care to better serve patients.

Beyond this foundational cultural element, the task force also identified three key domains or pillars (Figure) essential for cultivating high-quality, patient-centered care. Although programs appropriate for a Centers of Excellence designation might not possess mastery in all pillars, there must be a demonstrable investment in the pursuit of excellence across as many of these areas as a program can sustainably achieve, including the following pillars:

- **Education and training.** Delivering comprehensive patient and care-partner education and training, fostering staff training and continuous education, and an investment in fostering future leaders in the home dialysis space for programs with established nephrology fellowship training programs.
- **Infrastructure and care delivery.** Demonstrating clear leadership and excellent communication across the multidisciplinary team, with internal processes and external partnerships in place to support sustainable, patient-centered home dialysis care.
- **Quality improvement and assurance.** Focusing on ongoing systematic processes for monitoring, evaluating, and enhancing the quality and safety of home dialysis care.

Figure. Pillars for delivering high-quality, patient-centered care



Next steps and community engagement

The work of the Centers of Excellence in Home Dialysis Task Force so far has primarily involved subject matter experts from within the home dialysis community. The program is now entering a crucial phase of broader stakeholder engagement. The task force plans to gather feedback directly from patients on home dialysis through organized discussions. This direct patient and care-partner input is critical for ensuring that the proposed blueprint for a Centers of Excellence designation accurately reflects patients' experiences and addresses their needs and priorities.

Following the integration of patient perspectives, this initial blueprint will be piloted in collaboration with a small number of interested programs, refined, and then presented to the larger nephrology community for comprehensive consideration and feedback. This practical approach is intended to ensure that no key components of highly effective programs are omitted from consideration for the Centers of Excellence designation criteria. Furthermore, this pilot will offer opportunities to collaborate with the nephrology community to refine the process and criteria for programs interested in pursuing and receiving a Centers of Excellence designation.

Ultimately, ASN's Centers of Excellence in Home Dialysis program represents a significant initiative aimed at defining, recognizing, and promoting the highest standards of home dialysis care with the overarching goals of improving access, quality of care, and quality of life for people living with kidney failure. ■

Edward Gould, MD, FASN, is chair of the ASN Centers of Excellence in Home Dialysis Task Force, chief of medicine at the Nashville VA Medical Center, and an assistant professor of medicine at Vanderbilt University School of Medicine, Nashville, TN. Kerry Leigh, BSN, RN, is a senior clinical nurse program manager at ASN and staff liaison to the Centers of Excellence in Home Dialysis Task Force.

The authors report no conflicts of interest.

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Reduction in Blood Pressure with Ultrasound Renal Denervation: Real-World results from a Single Center Experience.

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Introduction

Hypertension remains the leading cause of death worldwide despite readily available treatment options. Renal denervation (RDN) has been shown to be effective in reducing blood pressure in patients with resistant hypertension in multiple clinical trials.

Renal denervation

The Paradise® Ultrasound RDN procedure uses high-frequency ultrasound to ablate renal nerves. This study presents a real-world experience with ultrasound RDN for the treatment of resistant hypertension at a single center.

Hypothesis

We assessed the hypothesis that the Paradise® Ultrasound RDN System would provide a safe and effective approach to reduce systolic blood pressure (SBP) in patients with resistant hypertension.

Methods

Twenty consecutive patients were treated with the Paradise Ultrasound RDN System at Mon Health Medical Center between December 2023 and September 2024. Patients had office SBP 167 mmHg despite optimized antihypertensive therapy. Office SBP was measured at baseline and at follow-up visits at regular intervals post-RDN procedure.

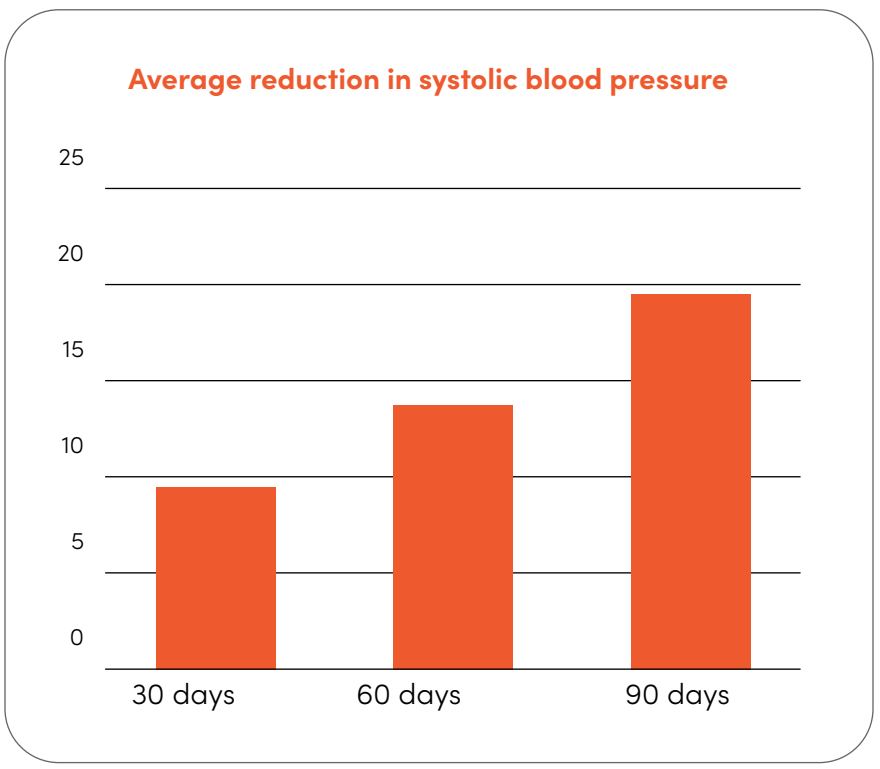
Results

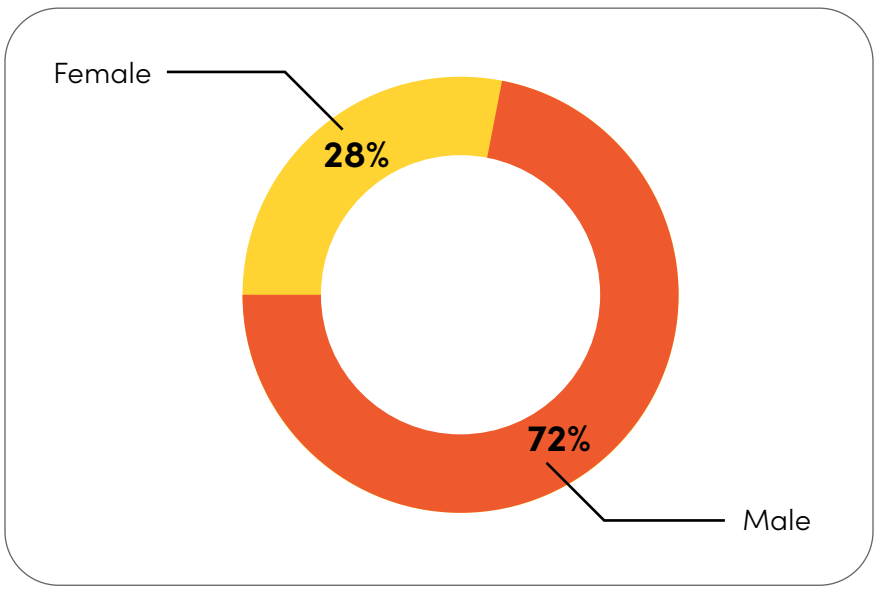
At 90 days post-RDN procedure:

- Mean office SBP was reduced by an average of -19 mmHg compared to baseline
- At 6-months of follow up the average OBP was 154/82 mmHg
- No major adverse events were reported

Conclusion

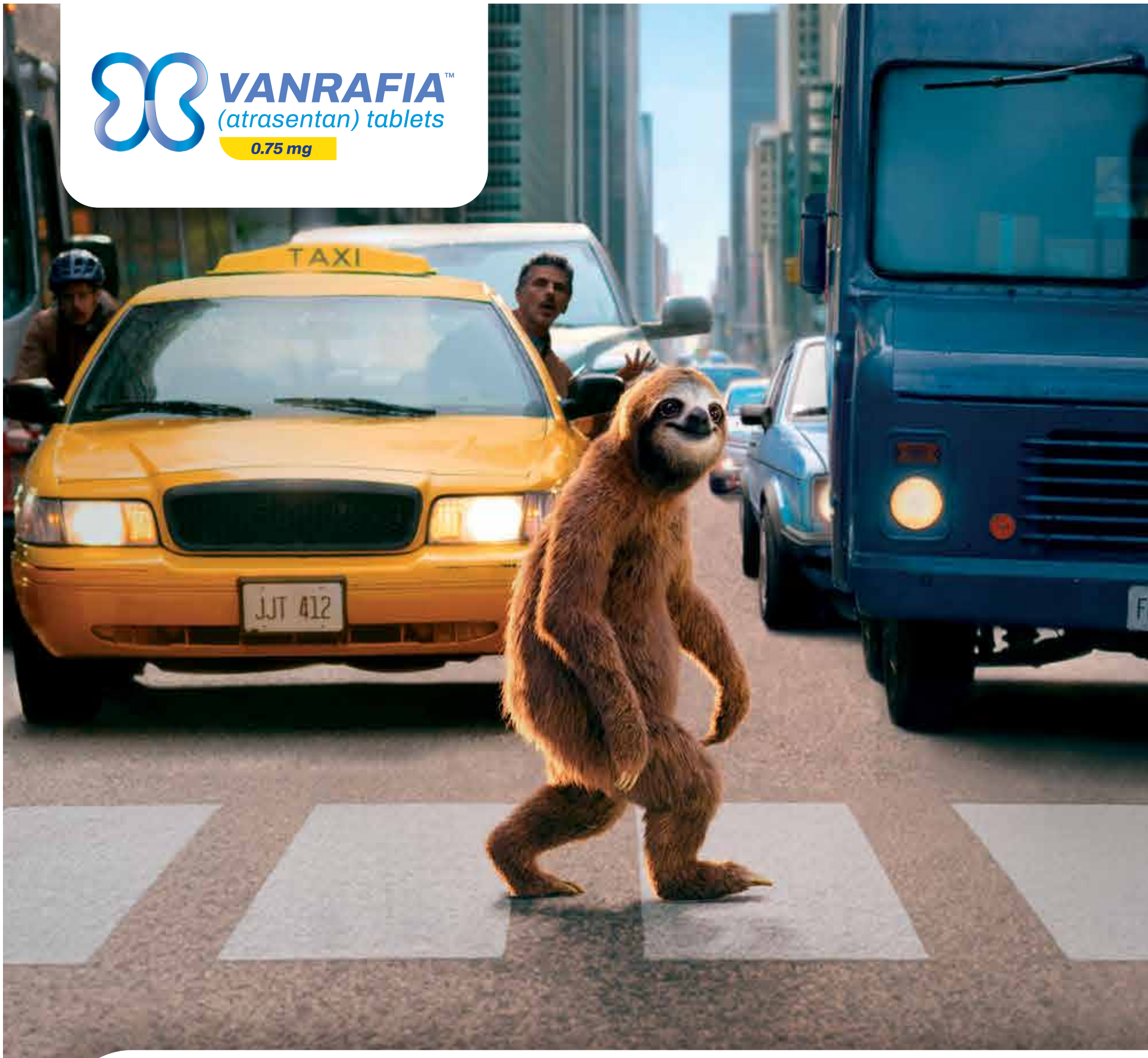
Ultrasound RDN offers patients with resistant hypertensive a promising treatment option. This study demonstrates that ultrasound RDN is safe and effective for reducing blood pressure in real-world clinical practice with no major adverse events.





Scan the code to view Important Safety Information

The most common risks include pain, vascular access site complications and vasospasm.



INDICATION

VANRAFIA is 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 of proteinuria. It has not been established whether VANRAFIA 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

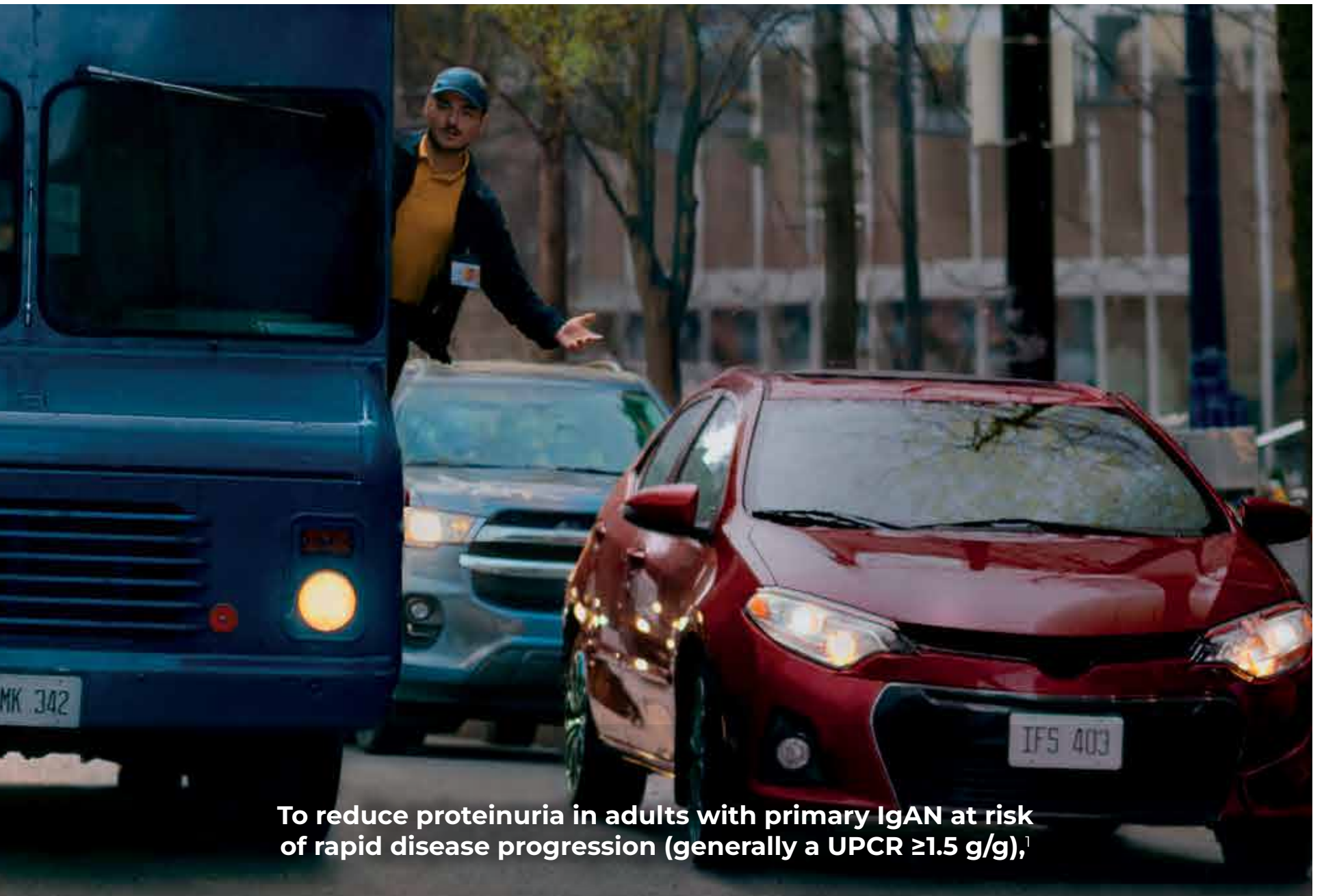
WARNING: EMBRYO-FETAL TOXICITY

VANRAFIA is contraindicated for use in pregnant patients; it may cause major birth defects, based on animal data. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise use of effective contraception before the initiation of treatment, during treatment, and for 2 weeks after discontinuation of treatment with VANRAFIA. Stop VANRAFIA as soon as possible if the patient becomes pregnant.

CONTRAINDICATIONS

Pregnancy

Use of VANRAFIA is contraindicated in patients who are pregnant.



To reduce proteinuria in adults with primary IgAN at risk of rapid disease progression (generally a UPCR ≥1.5 g/g),[1]

IT'S TIME TO MOVE A LITTLE FASTER

Consider solidifying your foundation with a single addition to RASi ± SGLT2i for appropriate patients. **Add on VANRAFIA® (atrasentan)**[1]

IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS (continued)

Hypersensitivity

VANRAFIA is contraindicated in patients with a history of a hypersensitivity reaction to atrasentan or any component of the product.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

Based on data from animal reproduction studies, VANRAFIA may cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. The available human data for endothelin receptor antagonists (ERAs) do not establish the presence or absence of major birth defects related to the use of VANRAFIA. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise patients to use effective contraception prior to initiation of treatment, during treatment, and for 2 weeks after discontinuation of treatment with VANRAFIA. When pregnancy is detected, discontinue VANRAFIA as soon as possible.

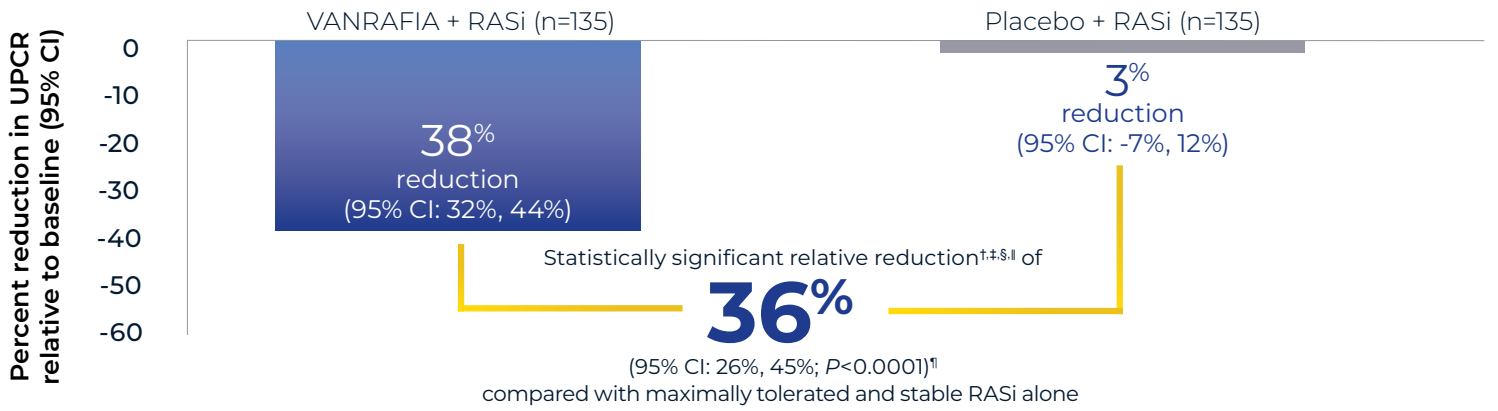
Please see additional Important Safety Information and Brief Summary of full Prescribing Information, including Boxed WARNING, on the following pages.

When added to a maximally tolerated and stable RASi regimen,

VANRAFIA delivered a significant reduction in UPCR at Week 36 for patients with IgAN in the main cohort (n=270)[1,2]

The ALIGN clinical trial is an ongoing, phase 3, global, multicenter, randomized, double-blind, placebo-controlled study assessing the efficacy and safety of VANRAFIA in combination with a maximally tolerated and stable dose of RASi in IgAN. An additional exploratory SGLT2i cohort of 64 patients who were also on a stable dose of an SGLT2i at baseline was enrolled.

PERCENT REDUCTION IN UPCR FROM BASELINE AFTER 9 MONTHS OF TREATMENT*,†



- Patients in both the VANRAFIA and placebo groups were on a **maximally tolerated and stable dose of RASi** at baseline that was continued throughout the duration of the study

- The ALIGN trial assessed a separate exploratory SGLT2i cohort of 64 patients who were on a maximally tolerated and stable RASi + SGLT2i. The exploratory efficacy analysis was based on 29 of these patients who reached the Week 36 visit
- Preliminary findings from the interim exploratory analysis at 9 months showed consistent reductions in UPCR in patients on VANRAFIA + RASi + SGLT2i, with a 39.6% (95% CI: -54.1%, -20.4%) LS mean reduction from baseline vs a 3.4% (95% CL: -26.3%, 26.5%) reduction with RASi + SGLT2i alone#

Adverse reactions reported in ≥2% of adult patients with IgAN treated with VANRAFIA and higher than placebo in ALIGN**,††

Adverse reaction	VANRAFIA + RASi ± SGLT2i (N=201), n (%)	Placebo + RASi ± SGLT2i (N=202), n (%)
Peripheral edema[a]	**21 (10)**	**14 (7)**
Anemia[a]	**12 (6)**	**2 (1)**
Liver transaminase elevation[b]	**4 (2)**	**2 (1)**

[a]Includes related terms.
[b]Elevations in ALT or AST >3-fold ULN.

- Do not initiate VANRAFIA if your patient is pregnant and advise them to use effective contraception before, during, and for 2 weeks following discontinuation of treatment. Stop VANRAFIA as soon as possible if your patient becomes pregnant
- Similar to other endothelin receptor antagonists, VANRAFIA may have a reversible adverse effect on sperm count. Counsel male patients about potential effects on fertility. A decrease in sperm count in some patients with diabetic kidney disease has been observed with VANRAFIA, with normal levels returning within ~3 months of discontinuation. This effect has not yet been studied in patients with IgAN

ALT, alanine aminotransferase; AST, aspartate aminotransferase; LS, least squares; ULN, upper limit of normal.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hepatotoxicity

Some ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. Asymptomatic and transient transaminase elevations have been observed with VANRAFIA. Obtain liver enzyme testing before initiating VANRAFIA, and repeat during treatment as clinically indicated. In patients with elevated aminotransferases at baseline (>3 × upper limit of normal [ULN]), consider periodic liver test monitoring. Do not initiate VANRAFIA in patients with severe hepatic impairment.

Advise patients to report symptoms suggesting hepatic injury (eg, nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching). If clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 × ULN, or by clinical symptoms of hepatotoxicity, discontinue VANRAFIA. Consider reinitiation of VANRAFIA when hepatic enzyme levels normalize in patients who have not experienced clinical symptoms of hepatotoxicity or jaundice.

SOLIDIFY YOUR FOUNDATION WITH VANRAFIA

VANRAFIA + maximally tolerated and stable RASi provided greater total reduction in 24-hour UPCR compared with maximally tolerated and stable RASi alone, with a 38% (95% CI: 32%, 44%) reduction from baseline in the treatment arm vs only 3% (95% CI: -7%, 12%) in the placebo arm.[1,*,†]

RAPID AND SUSTAINED PROTEINURIA REDUCTION[1]

Improvements were seen as early as Week 6 and sustained through Month 9. **At Month 9, VANRAFIA achieved** a statistically significant relative reduction[†,‡,§,ǁ] of 24-hour UPCR compared with a maximally tolerated and stable RASi alone of 36% (95% CI: 26%, 45%; *P*<0.0001)[¶] relative to baseline

FIRST AND ONLY ET_A RECEPTOR ANTAGONIST IN IgAN WITHOUT A REMS PROGRAM[1]

Use of VANRAFIA is contraindicated in patients who are pregnant and patients with hypersensitivity. Serious warnings associated with VANRAFIA include embryo-fetal toxicity, hepatotoxicity, fluid retention, and decreased sperm counts. Most common adverse reactions (incidence ≥5%) were peripheral edema and anemia. Please see additional Important Safety Information throughout

TARGETS THE ET_A RECEPTOR. NOT A STEROID[1]

VANRAFIA is an ET_A receptor antagonist that can be added to your patient's maximally tolerated and stable RASi ± SGLT2i

Solidify your foundation with a single addition to RASi ± SGLT2i for appropriate patients.
ADD ON VANRAFIA[1]

Download the start form
at VANRAFIA-startform.com

*LS geometric mean ratio in UPCR (sampled from a 24-hour urine collection) to baseline was reported as a percent reduction along with the respective 95% CI.[1] †MMRM analysis included all observed UPCR data except for subjects with intercurrent events (eg, restricted medication use, chronic dialysis, kidney transplant). These subjects had UPCR data excluded beginning at the start date of the earliest event. The only intercurrent events observed were restricted medication use, which occurred in 3.0% and 5.2% of VANRAFIA- and placebo-treated subjects, respectively.[1,2] ‡Statistically significant results coming from an interim analysis for accelerated approval through 36 weeks of treatment. The study for full approval is ongoing and will be based on data from 132 weeks of treatment.[1,2] §The estimate of the ratio of LS geometric mean ratio in UPCR (sampled from a 24-hour urine collection) to baseline comparing VANRAFIA with placebo was reported as a relative percent reduction along with the respective 95% CI and 2-sided *P* value.[1] ǁThe relative percent difference between VANRAFIA and placebo is equal to the ratio of the geometric mean minus 1 multiplied by 100: 100*[(0.62/0.97)-1]= -36%.[1] ¶Two-sided *P* value statistically significant at the 0.01 level.[1] #Limitations: In ALIGN, UPCR was observed in an exploratory cohort of patients on RASi + SGLT2i treatment at study start. No clinical or statistical conclusions can be drawn. Results cannot be generalized to patients with total urine protein <1 g/day. Underrepresentation of Black patients limits generalizability to these patients.[2] **The safety analysis was based on patients from both cohorts (n=403) for the duration that they received VANRAFIA.[1] ††The median duration of treatment was 47 weeks (range: 0 to 128 weeks).[1]

ET_A, endothelin A; MMRM, mixed model of repeated measures; REMS, Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Fluid Retention

Fluid retention may occur with ERAs and has been observed in clinical studies with VANRAFIA. VANRAFIA has not been evaluated in IgAN patients with heart failure. If clinically significant fluid retention develops, consider initiating or increasing diuretic treatment and interrupting VANRAFIA treatment.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information, including Boxed WARNING, on the following pages.

VANRAFIA™ (atrasentan) tablets 0.75 mg

Indication and Important Safety Information

INDICATION

VANRAFIA is 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.

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IMPORTANT SAFETY INFORMATION

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CONTRAINDICATIONS

Pregnancy

Use of VANRAFIA is contraindicated in patients who are pregnant.

Hypersensitivity

VANRAFIA is contraindicated in patients with a history of a hypersensitivity reaction to atrasentan or any component of the product.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

Based on data from animal reproduction studies, VANRAFIA may cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. The available human data for endothelin receptor antagonists (ERAs) do not establish the presence or absence of major birth defects related to the use of VANRAFIA. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise patients to use effective contraception prior to initiation of treatment, during treatment, and for 2 weeks after discontinuation of treatment with VANRAFIA. When pregnancy is detected, discontinue VANRAFIA as soon as possible.

Hepatotoxicity

Some ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. Asymptomatic and transient transaminase elevations have been observed with VANRAFIA. Obtain liver enzyme testing before initiating VANRAFIA, and repeat during treatment as clinically indicated. In patients with elevated aminotransferases at baseline (>3 × upper limit of normal [ULN]), consider periodic liver test monitoring. Do not initiate VANRAFIA in patients with severe hepatic impairment.

Advise patients to report symptoms suggesting hepatic injury (eg, nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching). If clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 × ULN, or by clinical symptoms of hepatotoxicity, discontinue VANRAFIA. Consider reinitiation of VANRAFIA when hepatic enzyme levels normalize in patients who have not experienced clinical symptoms of hepatotoxicity or jaundice.

Fluid Retention

Fluid retention may occur with ERAs and has been observed in clinical studies with VANRAFIA. VANRAFIA has not been evaluated in IgAN patients with heart failure. If clinically significant fluid retention develops, consider initiating or increasing diuretic treatment and interrupting VANRAFIA treatment.

Decreased Sperm Counts

VANRAFIA, similar to other ERAs, may have an adverse effect on spermatogenesis. Counsel men about the potential effects on fertility.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥5%) with VANRAFIA were peripheral edema and anemia.

EFFECT OF OTHER DRUGS ON VANRAFIA

Strong or Moderate CYP3A Inducers: Avoid concomitant use with a strong or moderate CYP3A inducer. Atrasentan is a CYP3A substrate. Concomitant use with a strong and moderate CYP3A inducer is expected to decrease atrasentan exposure, which may reduce VANRAFIA efficacy.

OATP1B1/1B3 Inhibitors: Avoid concomitant use with organic anion transporting polypeptides (OATP) 1B1/1B3 (OATP1B1/1B3) inhibitors. Atrasentan is an OATP1B1/1B3 substrate. Concomitant use with an OATP1B1/1B3 inhibitor increases atrasentan exposure, which may increase the risk of VANRAFIA adverse reactions.

Please see Brief Summary of full Prescribing Information, including Boxed WARNING, on the right page.

References: 1. Vanrafia. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Heerspink HJL, Jardine M, Kohan DE, et al. Atrasentan in patients with IgA nephropathy. *N Engl J Med.* 2025;392(6):544-554. doi:10.1056/NEJMoa2409415

NOVARTIS

VANRAFIA™ (atrasentan) tablets 0.75 mg

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Printed in USA 7/25 418924

VANRAFIA™ (atrasentan) tablets, for oral use
Initial U.S. Approval: 2025

BRIEF SUMMARY: Please see package insert for full prescribing information.

WARNING: EMBRYO-FETAL TOXICITY

VANRAFIA is contraindicated for use in pregnant patients; it may cause major birth defects based on animal data *[see Contraindications (4.1), Warnings and Precautions (5.1), Use in Specific Populations (8.1)]*. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise use of effective contraception before the initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with VANRAFIA. Stop VANRAFIA as soon as possible if the patient becomes pregnant *[see Dosage and Administration (2.1) in the full prescribing information, Contraindications (4.1), Warnings and Precautions (5.1), Use in Specific Populations (8.1, 8.3)]*.

1 INDICATIONS AND USAGE

VANRAFIA is 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 of proteinuria *[see Clinical Studies (14.1) in the full prescribing information]*. It has not been established whether VANRAFIA 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.

4 CONTRAINDICATIONS

4.1 Pregnancy

Use of VANRAFIA is contraindicated in patients who are pregnant *[see Dosage and Administration (2.1) in the full prescribing information, Warnings and Precautions (5.1), Use in Specific Populations (8.1)]*.

4.2 Hypersensitivity

VANRAFIA is contraindicated in patients with a history of a hypersensitivity reaction to atrasentan or any component of the product.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

Based on data from animal reproduction studies, VANRAFIA may cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. The available human data for endothelin receptor antagonists do not establish the presence or absence of major birth defects related to the use of VANRAFIA. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy prior to initiation of treatment with VANRAFIA. Advise patients to use effective contraception prior to initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with VANRAFIA *[see Dosage and Administration (2.1) in the full prescribing information and Use in Specific Populations (8.1, 8.3)]*. When pregnancy is detected, discontinue VANRAFIA as soon as possible *[see Dosage and Administration (2.1) in the full prescribing information, Contraindications (4.1), Use in Specific Populations (8.1, 8.3)]*.

5.2 Hepatotoxicity

Some endothelin receptor antagonists (ERAs) have caused elevations of aminotransferases, hepatotoxicity, and liver failure. Asymptomatic and transient transaminase elevations have been observed with VANRAFIA *[see Adverse Reactions (6.1)]*. Obtain liver enzyme testing before initiating VANRAFIA and repeat during treatment as clinically indicated. In patients with elevated aminotransferases at baseline (>3 × upper limit of normal [ULN]), consider periodic liver test monitoring. Do not initiate VANRAFIA in patients with severe hepatic impairment.

Advise patients to report symptoms suggesting hepatic injury (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching). If clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or by clinical symptoms of hepatotoxicity, discontinue VANRAFIA. Consider re-initiation of VANRAFIA when hepatic enzyme levels normalize in patients who have not experienced clinical symptoms of hepatotoxicity or jaundice.

5.3 Fluid Retention

Fluid retention may occur with ERAs and has been observed in clinical studies with VANRAFIA *[see Adverse Reactions (6.1)]*. VANRAFIA has not been evaluated in IgAN patients with heart failure. If clinically significant fluid retention develops, consider initiating or increasing diuretic treatment and interrupting VANRAFIA treatment.

5.4 Decreased Sperm Counts

VANRAFIA, similar to other ERAs, may have an adverse effect on spermatogenesis. Counsel men about potential effects on fertility *[see Use in Specific Populations (8.3) and Nonclinical Toxicology (13.1) in the full prescribing information]*.

6 ADVERSE REACTIONS

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

- Embryo-fetal Toxicity *[see Warnings and Precautions (5.1)]*
- Hepatotoxicity *[see Warnings and Precautions (5.2)]*
- Fluid Retention *[see Warnings and Precautions (5.3)]*
- Decreased Sperm Counts *[see Warnings and Precautions (5.4)]*

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 VANRAFIA was evaluated in ALIGN (NCT04573478), a randomized, double-blind, placebo controlled clinical study in 403 adults with IgAN *[see Clinical Studies (14.1) in the full prescribing information]*. The median duration of treatment was 47 weeks (range: 0 to 128 weeks). The most common adverse reactions (≥ 5%) with VANRAFIA were peripheral edema and anemia. Table 1 describes the adverse reactions that occurred in ≥ 2% of patients treated with VANRAFIA and higher than placebo in the ALIGN study.

Table 1: Adverse Reactions Reported in ≥ 2% of Adult Patients with IgAN Treated with VANRAFIA and Higher than Placebo in ALIGN

Adverse Reaction	VANRAFIA (N = 201) n (%)	Placebo (N = 202) n (%)
Peripheral edema*	21 (10%)	14 (7%)
Anemia*	12 (6%)	2 (1%)
Liver transaminase elevation**	4 (2%)	2 (1%)

* Includes related terms
**Elevations in ALT or AST > 3-fold upper limit of normal (ULN)

Laboratory Tests and Vital Signs

Hemoglobin Decrease

At Week 36, the mean change in hemoglobin from baseline for those patients receiving VANRAFIA in the ALIGN study was -0.7 g/dL compared to -0.2 g/dL for those receiving placebo. The incidence of a hemoglobin decrease > 2 g/dL compared to baseline and below the lower limit of normal was greater for the VANRAFIA arm (12%) compared to the placebo arm (4%). These decreases are thought to be in part due to hemodilution. There were no treatment discontinuations due to anemia or hemoglobin decrease in the ALIGN study.

Blood Pressure Decrease

At Week 36, the mean change from baseline in systolic and diastolic blood pressure (BP) for patients receiving VANRAFIA in the ALIGN study was -4 mmHg and -4 mmHg, respectively, compared to +3 mmHg and +2 mmHg, respectively, in patients receiving placebo. Hypotension observed in VANRAFIA treated patients was mild or moderate in severity, rarely symptomatic, and did not necessitate treatment discontinuation.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on VANRAFIA

Strong or Moderate CYP3A Inducers

Avoid concomitant use with a strong or moderate CYP3A inducer.

Atrasentan is a CYP3A substrate *[see Clinical Pharmacology (12.3) in the full prescribing information]*. Concomitant use with a strong and moderate CYP3A inducer is expected to decrease atrasentan exposure *[see Clinical Pharmacology (12.3) in the full prescribing information]*, which may reduce VANRAFIA efficacy.

OATP1B1/1B3 Inhibitors

Avoid concomitant use with organic anion transporting polypeptides 1B1/1B3 (OATP1B1/1B3) inhibitors.

Atrasentan is a OATP1B1/1B3 substrate *[see Clinical Pharmacology (12.3) in the full prescribing information]*. Concomitant use with a OATP1B1/1B3 inhibitor increases atrasentan exposure *[see Clinical Pharmacology (12.3) in the full prescribing information]*, which may increase the risk of VANRAFIA adverse reactions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on data from animal reproductive toxicity studies, VANRAFIA may cause fetal harm, including birth defects and fetal death, when administered to a pregnant patient and is contraindicated during pregnancy *[see Contraindications (4.1)]*. There are no available data on VANRAFIA use in pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Available data from published literature and post-marketing surveillance over decades of use with products in the same pharmacologic class (ERA) have not identified an increased risk of major birth defects. However, these data are limited and do not establish the presence or absence of a drug-associated risk of major birth defects. Methodological limitations of these post marketing reports and published literature include lack of a control group; limited information regarding dose, duration, and timing of exposure; and missing data. These limitations preclude establishing a reliable estimate of the risk of adverse fetal and neonatal outcomes with maternal endothelin receptor antagonist use.

In animal reproduction studies, oral administration of atrasentan to pregnant rats and rabbits throughout organogenesis at doses that were below the maximum recommended human dose (MRHD) based on area under the curve (AUC) caused teratogenic effects in rats and rabbits *(see Data)*. Advise pregnant patients of the potential risk to the fetus *[see Contraindications (4.1)]*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, 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.

Data

Animal Data

In embryo-fetal development studies in pregnant rats and rabbits, teratogenicity and/or embryo-fetal toxicity were observed.

In pregnant rats, oral administration of atrasentan throughout organogenesis at doses of 0.1, 0.3, 1.0, and 3.0 mg/kg/day resulted in developmental abnormalities primarily including the ear, lower jaw, or skull in all treated groups with detectable plasma exposures to atrasentan. The no adverse effect level of atrasentan plasma exposure was not determined. In pregnant rabbits, oral administration of atrasentan throughout organogenesis at doses of 0.1, 0.3, 1.0 and 3.0 mg/kg/day resulted in visceral malformations including deformities in the cardiovascular system in all atrasentan-treated groups. The lowest detectable plasma exposures to atrasentan were approximately 0.2 times the AUC at the MRHD.

In the pre- and postnatal development study in rats, atrasentan was orally administered to pregnant rats at doses of 1, 10, or 100 mg/kg/day during the period from gestation Day 15 through lactation Day 20. No adverse effects on pre- and postnatal development were observed at doses up to 10 mg/kg/day which resulted in maternal exposure approximately 55 times the AUC at the MRHD. Higher exposure to atrasentan (dose of 100 mg/kg/day) increased pup mortality during the pre-weaning period, and increased heart weight which correlated histologically with myocardial hypertrophy.

8.2 Lactation

Risk Summary

There are no data on the presence of atrasentan in human milk, the effects on the breastfed infant, or the effect on milk production. Because of the potential for adverse reactions, such as fluid retention in breastfed infants, advise patients not to breastfeed during treatment with VANRAFIA.

8.3 Females and Males of Reproductive Potential

Based on data from animal reproductive toxicity studies, VANRAFIA may cause fetal harm, including birth defects and fetal death, when administered to a pregnant patient and is contraindicated during pregnancy *[see Contraindications (4.1), Use in Specific Populations (8.1)]*.

Pregnancy Testing

Exclude pregnancy before initiating VANRAFIA in females of reproductive potential. The patient should contact their physician immediately for pregnancy testing if onset of menses is delayed or pregnancy is suspected. If pregnancy is confirmed, the physician should discuss with the patient the risks to the pregnancy and the fetus.

Contraception

Patients who can become pregnant while using VANRAFIA should use effective contraception prior to initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with VANRAFIA to prevent pregnancy *[see Warnings and Precautions (5.1)]*.

Infertility

Decreased sperm counts have been observed in some patients with diabetic kidney disease (DKD) receiving VANRAFIA 0.75 mg once daily with return to normal levels within approximately 3 months after drug discontinuation. This effect has not been studied in patients with IgAN *[see Nonclinical Toxicology (13.1) in the full prescribing information]*.

8.4 Pediatric Use

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

8.5 Geriatric Use

There were 29 (7%) patients 65 years of age and older in the ALIGN study of VANRAFIA. Of the total number of VANRAFIA-treated patients, 15 (7%) were 65 years to 75 years of age, and 3 (2%) were 75 years of age and older. No overall differences in safety and effectiveness were observed between these patients and younger patients.

8.6 Hepatic Impairment

No dose adjustment is required for patients with mild or moderate hepatic impairment. Do not initiate VANRAFIA in patients with severe hepatic impairment *[see Warnings and Precautions (5.2)]*.

10 OVERDOSAGE

There is no experience with overdose of VANRAFIA. Atrasentan has been given in a single dose up to 139.5 mg and multiple doses up to 40 mg/day in healthy volunteers. Overdose of VANRAFIA may result in headache or vasodilation. In the event of an overdose, standard supportive measures should be taken, as required. Dialysis is unlikely to be effective because atrasentan is highly protein-bound.

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T2025-18

Building a Unified Future: The ASN Journal Portfolio 2 Years In

https://doi.org/10.62716/kn.002002025

The ASN Journal Portfolio (*JASN*, *CJASN*, and *Kidney360*) is led by Rajnish Mehrotra, MD, MS, FASN, who also serves as editor-in-chief (EIC) of *JASN*, along with EIC of *CJASN* Connie Rhee, MD, MSc, and EIC of *Kidney360* Michael Allon, MD. Each ASN journal provides a unique focus on the practice and research of nephrology—publishing breaking clinical and basic research, editorials, perspectives, reviews, podcasts, and more—while enabling a consistent experience and shared vision under one portfolio. Nearly 2 years after assuming the role, Mehrotra spoke with *Kidney News* (*KN*) about the success and future goals of the portfolio.

KN: By the time of publication, you will have served as the inaugural senior EIC of the ASN Journal Portfolio for almost 2 years, in addition to serving as EIC of *JASN*. How has this structure been working?

Mehrotra: I want to thank the ASN Council and the Publications Committee for entrusting me with the responsibility of serving as the inaugural senior EIC of the ASN Journal Portfolio (*JASN*, *CJASN*, and *Kidney360*). While each journal continues to be led by its own editorial team, the portfolio structure was established to increase collaboration, communication, and harmonization among the three journals. The overarching goal is to better serve our readers by publishing a wider range of the highest-quality scientific content while reducing redundancy among the journals.

The first year and a half of us working together within the portfolio structure has been incredibly productive. This has been possible because of the strong support and partnership with Drs. Rhee and Allon, EICs of *CJASN* and *Kidney360*, respectively; the ASN Publications team led by Bob Henkel and Shari Leventhal; and the managing editors of the three journals (Natalie Ngo, Sydney Cough, and Kim Stuart). We have established a regular cadence of team meetings to set strategic priorities and directions and review progress for the portfolio.

In the first year, we focused on establishing a shared portfolio infrastructure with a lead statistical editor (Patrick Heagarty, PhD, MS) and pool of statistical reviewers, a lead visual abstract editor (Edgar Lerma, MD, FASN) and pool of visual abstract editors, a lead communications editor (Matthew Sparks, MD, FASN), and a single editorial board. We also harmonized the author and reviewer experience across the journals. In this second year, we have set shared standards for data presentation for both basic and clinical research in the journals, and we are now refining our process for transferring manuscripts from one journal to another.

KN: What are some of the benefits of this portfolio structure to authors, reviewers, and readers?

Mehrotra: We hope that authors around the world submit their highest-impact kidney-related research to one of the ASN journals. To attract such work, we have reduced the burden of submission for authors. We have harmonized article specifications to be identical across the journals and no longer require journal-specific formatting at initial submission. Authors simply upload the manuscript as a Word document, and the submission system extracts information such as the title and abstract to automatically populate the fields. We do not ask authors to complete an article-type–specific checklist, as it is completed by the associate editor at the time of initial decision if we invite a revision. We do not ask for authors' copyrights or disclosure forms at initial submission either. Authors do not have to create their own visual abstracts; instead, our team of visual abstract editors creates them for the authors to review. We provide timely and thoughtful decisions to authors, such that we render an initial decision (to send out for external review or not) within 5 days and for manuscripts sent out for external review, within 30 days.

Harmonizing article specifications and submission forms across the portfolio has also facilitated a streamlined transfer process among the ASN journals. At the time of initial submission, authors can indicate if they wish to transfer the manuscript to another ASN journal if the first journal does not advance the manuscript. The transfer process is completed within 1 business day of the editorial decision and does not require any action from the authors. If granted permission, reviewers' comments are transferred to the receiving journal as well, which significantly shortens the decision time at the receiving journal and reduces the demands on our reviewers.

The portfolio structure has also allowed us to have a single pool of reviewers across the journals, expanding the breadth and depth of experts available for peer review and reducing reviewer burnout. We are deeply appreciative of our reviewers. Between January 2024 and August 2025, more than 3600 individuals from around the world volunteered as reviewers to help editors assess the scientific rigor and validity of research work submitted to the ASN journals. Establishing a single pool of reviewers helps us avoid inconveniencing busy researchers with simultaneous review requests from different ASN journals. As mentioned earlier, our ability to transfer manuscripts between journals with reviews from the transferring journal further reduces the demands on reviewers' time.

The portfolio has expanded the modes of dissemination of the content we publish to amplify and diversify access to our readers and authors. Each journal publishes visual abstracts created by our editors for all original research articles and selects one article for a podcast every month. Last year, we introduced the Kidney Translation Podcast series, a portfolio-wide podcast led by Matthew Sparks. Each episode features a different theme, highlighting an article from each journal. Additionally, our publisher Wolters Kluwer added a Read Out Loud tool that allows readers to listen to a transcript of the work. Wolters Kluwer also recently added plain-language summaries to online articles to further extend the reach of the work we publish. To further serve our authors and readers, we have expanded our social media presence to include Bluesky and transitioned to one ASN Publications X (formerly Twitter) account that features the latest content published by all four ASN publications (including *Kidney News*). With 31,000+ followers on X and close to 1000 followers on Bluesky, we continue to actively disseminate our published content with new audiences.

Collectively, we hope that these changes have improved the experience of authors, reviewers, and readers of the ASN journals.

KN: You served 7 years as EIC of *CJASN* prior to becoming EIC of *JASN* 2 years ago. With that unique perspective, how do you think kidney research has changed over the past 9 years?

Mehrotra: The most striking "big picture" change of course is the increasing sophistication of approaches for hypothesis testing, both in basic science and clinical research. This is reflected in the growing sophistication of research tools as well as research methods. The hope is that this increasing sophistication and scientific rigor translate into greater validity and reproducibility of research findings and accelerate progress in improving the lives of people living with kidney diseases.

More specifically, there has been an explosion of therapeutics for kidney diseases such as diabetic kidney disease and glomerular diseases, particularly for IgA nephropathy. There is a growing number of clinical trials and analysis of real-world data to help us better understand the efficacy, safety, and clinical applications of these advances in therapeutics. There is also a greater focus on patient-reported outcomes and on incorporating the patient voice and experience into kidney disease-related research.

I applaud and welcome all these changes, and I hope these advances collectively help us advance ASN's vision of a world without kidney diseases.

KN: Scientific and medical research in the United States is facing unprecedented challenges with federal policy changes affecting if and how research is conducted and published. How is the ASN Journal Portfolio upholding research integrity and engendering public trust in scholarly research and communications?

Mehrotra: It is ironic that at this time of increasing scientific rigor and therapeutic advances, public trust in biomedical research has declined. This erosion in public trust has far-reaching consequences, ranging from treatment decisions made by large segments of the population for themselves or by health care practitioners for their patients to public support for research funding such as in the United States.

Scholarly journals have an important responsibility in stemming and hopefully reversing this erosion in public trust, and ASN Publications takes this responsibility very seriously. We work hard to ensure the internal and external validity of the research that we publish by adhering to the highest standards for peer review and data presentation. We are increasingly intentional in asking authors to attest that their research followed international standards, such as the Declaration of Helsinki and the Declaration of Istanbul, and include a formal declarative statement in the published article. We expect researchers to share data with other researchers to support reproducibility. For clinical trials, we have long required the trials to be registered in a public trial registry, and now we ask authors to submit the prespecified statistical analysis plan with their initial submission. It is our goal that the work we publish is free of commercial bias, as even perception of financial conflict of interest is damaging. As such, we have streamlined the reporting of conflicts of interest through the ASN website and require authors to report all relationships. Rather than authors judging which relationships are important, we leave it to our readers. We publish all of the authors' disclosure forms with the online article for full transparency.

I acknowledge that we may still have process and procedural shortcomings within the portfolio, and we welcome our readers to help us identify and remedy them so that we can maximize the impact of advances in research for people living with kidney diseases.

KN: What are you most proud of in your tenure as senior EIC so far?

Mehrotra: I am most proud of the editorial teams that we have been able to assemble, tapping talent from around the world. Among the three journals, we have 56 editors (EICs, deputy editors, associate editors, and patient voice editors), 21 junior associate editors, 3 portfolio lead editors (communications, statistical, and visual abstract), 12 statistical reviewers, and 21 visual abstract editors. These are leaders in the field, recognized globally for their expertise, who have chosen to work with the ASN journals. It is the work that they do every day that has allowed us to accomplish all that we have, and I am immensely proud of their contributions and dedication.

KN: What can the kidney community expect from the ASN journals in the coming months and in 2026?

Mehrotra: We are excited to welcome the incoming EIC of *Kidney360*, Charuhas Thakar, MD, FASN. We look forward to working with him and identifying new ways to collaborate and enhance the experience of authors, reviewers, and readers. We have expanded our editorial training program to encompass all three journals. We now have 21 junior associate editors across the portfolio who are early career scientists being mentored as editors by senior associate editors on their journal's editorial teams. Additionally, each of the three journals will now award an annual Trainee of the Year award for the best original research with a trainee as the first author. But perhaps most importantly, it is the scientific advances that we publish in the ASN journals that have the potential to change the care and lives of people living with kidney diseases.

KidneyCure Pre-Doctoral Fellowship Program

The KidneyCure Pre-Doctoral Fellowship Program provides funding to early career-stage PhD students to conduct original research projects and make contributions to the understanding of kidney biology and disease.

Joanna Cunanan, MSc, BSc *
University Health Network
Mice With a Pax2 Missense Mutation are More Susceptible to Focal Segmental Glomerulosclerosis and Display Impaired Glomerular Repair

Isaac Karel, BA
The Ohio State University
A Novel Approach to Kidney Function Monitoring

Amanda Suda, MS *
University of Pittsburgh
Epithelial-derived miR-17~92 Regulates Jak/Stat, Serving in Female Renoprotection From Acute Kidney Injury

Ben J. Lipps Research Fellowship Program

The Ben J. Lipps Research Fellowship Program supports nephrology fellows who will advance the understanding of kidney biology and disease and is fully endowed by contributions provided by Fresenius Medical Care, ASN, the American Renal Patient Care Foundation, Inc., Vantive, and the PKD Foundation.

Joshua Carty, MD
Vanderbilt University Medical Center
Dissecting Energy Metabolism in the Regulation of Water Homeostasis
Ben J. Lipps Research Fellowship Award

Bernhard Dumoulin, MD *
University of Pennsylvania
Novel Approaches to Target B Cells in Chronic Kidney Disease
Ben J. Lipps Research Fellowship Award

Ali Etemadi, MD *
Stanford University
A Precision Medicine Approach to Optimizing Beta-Blocker Therapy in Hemodialysis
Dimitrios G. Oreopoulus Research Fellowship Award

Kashvi Gupta, MD, MPH
University of California San Francisco
Towards Better Blood Pressure Management Among Chronic Dialysis Patients
George B. Rathmann Research Fellowship Award

Stephanie Lapierre-Nguyen, PhD
University of Colorado, Denver
Inspiratory Muscle Strength Training for Improving Cerebrovascular and Cognitive Function in Midlife and Older Adults with Chronic Kidney Disease
Sharon Anderson Research Fellowship Award

Melina Messing, PhD *
University of California, Santa Barbara
Immune Mechanisms Underlying Efficacy of Ketogenic Metabolic Therapy in Polycystic Kidney Disease
Jared J. Grantham Research Fellowship Award

Brona Moloney, MB Bch BAO *
Brigham and Women's Hospital
Novel Volume Assessment Techniques for Predictive Cardiorenal Outcomes in High-Risk Cardiovascular Chronic Kidney Disease Patients in an Ambulatory Setting
Ben J. Lipps Research Fellowship Award

Ayodeji Oteyola, PhD, MS *
Albert Einstein College of Medicine
Atypical FAT1 Cadherin and Vascular Calcification in Chronic Kidney Disease
Donald E. Wesson Research Fellowship Award

Magdalena Riedl Khursigara MD, PhD
Broad Institute
Elucidating the Role of TMED7 in Trafficking of Misfolded Protein Mucin 1
Ben J. Lipps Research Fellowship Award

Elena Zion, MD
Boston Children's Hospital
AAV-based Gene Replacement Therapy in Mouse Models of RCAD Due to Hnf1b Loss
Ben J. Lipps Research Fellowship Award

Transition to Independence Grants Program

The Transition to Independence Grants Program helps young investigators achieve independent research careers and is supported by contributions provided by ASN, Akebia Therapeutics, Inc., Otsuka and Visterra, and individual donors.

Annabel Biruete, PhD
Purdue University
Dietary Fiber in Chronic Kidney Disease
Carl W. Gottschalk Research Scholar Grant

Robert Bronstein, PhD
Stony Brook University
Fosl2 Control of Epigenomic and Splicing Dynamics in Crescentic Glomerulopathies
Carl W. Gottschalk Research Scholar Grant

Denver Brown, MD
Children's Research Institution/Children's National Hospital-George Washington University
Metabolic Acidosis and Growth in a Heterogeneous Pediatric CKD Population: A Target Trial Emulation Study
KidneyCure Research Scholar Grant

Monica Chang-Panesso, MD
Washington University in St. Louis
Elucidating the Role of Metabolic Reprogramming in the Repair Capacity of the Aged Kidney
Carl W. Gottschalk Research Scholar Grant

Caroline Hsu, MD, MS
Tufts Medical Center
Peritoneal Dialysis in Hospitals and Skilled Nursing Facilities
Carl W. Gottschalk Research Scholar Grant

Gabriel Loeb, MD, PhD
University of California San Francisco
Identifying Novel Drivers of Kidney Disease Using Human Genetics
Carl W. Gottschalk Research Scholar Grant

Jonathan Nelson, PhD *
University of Southern California
Defining the Physiological Actions of the Interstitium
Carl W. Gottschalk Research Scholar Grant

Balaji Karthick Subramanian, PhD
Beth Israel Deaconess Medical Center
Tissue Chip System to Study Normal and Disease Podocyte Behaviors
Norman Siegel Research Scholar Grant

Hengcheng Zhang, MD, PhD
Bringham and Women's Hospital
The Role of Intrarenal T Follicular Helper Cells in Mediating Graft Dysfunction After Kidney Transplantation
John Merrill Grant in Transplantation

William and Sandra Bennett Clinical Scholars Program

The William and Sandra Bennett Clinical Scholars Program provides funding to clinician educators to conduct a project to advance all facets of nephrology education and teaching.

Sophia Ambruso, DO *
Rocky Mountain Regional VA Medical Center, University of Colorado School of Medicine
ABC Kidney - Development, Implementation and Assessment of a Gamified, Interactive Kidney Physiology Tutorial for Undergraduate Medical Education

** Kidney Week 2025 oral and/or poster abstract presenter*

CMV Viremia Risk in Hepatitis C-Infected Kidneys: Not So High After All

By Johnny Thornton, Mary Kate Kelly, and Sam Kant

https://doi.org/10.62716/kn.002182025

The growing shortage of organs has prompted transplant programs worldwide to re-examine long-held practices regarding donor selection, especially concerning organs from individuals infected with hepatitis C virus (HCV). Over the past decade, the successful use of direct-acting antivirals has revitalized interest in transplanting kidneys from donors who are HCV-viremic into recipients who are uninfected (HCV D+/R–), significantly expanding the donor pool. Yet, concerns have mounted regarding secondary infectious risks—most notably, the risk of cytomegalovirus (CMV) viremia in this unique population. HCV, especially after transplant, may transiently impair cellular immune responses, particularly a T cell-mediated defense. This could reduce the recipient's ability to control CMV replication, especially if there are delays in starting direct-acting antivirals.

A recently published multicenter retrospective cohort study brings clarity to this issue. The investigators analyzed data from five US transplant centers from 2015 to 2020, assembling a highly matched cohort of kidney recipients with HCV D+/R– and those with donors who were non–HCV-viremic (HCV D–/R–), with careful adjustment for center-specific practices, CMV donor/recipient serostatus, and antibody induction therapy. Specifically, the incidence of CMV viremia (>1000 IU/mL) was 15% in the HCV D+/R– group and 11% in the HCV D–/R– group. Adjusted Cox regression confirmed that HCV-RNA+ donor status did not carry a significant impact on CMV viremia risk (hazard ratio [HR], 1.30; 95% confidence interval [CI], 0.89–1.92) nor on the risk of death-censored graft loss (HR, 0.61; 95% CI, 0.31–1.20) (1). These findings are supported by other studies demonstrating similar short-term infectious risks and allograft outcomes, further reducing the concern for added infectious jeopardy in this population (2). The core finding: There was no statistically significant increase in CMV viremia among those who received HCV-viremic kidneys compared with those transplanted from donors who were nonviremic.

This study is valuable because previous analyses were limited by small numbers, center-specific practices, and insufficient power to address relevant confounders (3). The carefully matched design and multicenter scope of this cohort strengthen the generalizability of the results and offer reassurance to both clinicians and patients considering HCV D+/R– transplant. The study also contextualizes the risk of CMV in the era of universal or risk-based prophylaxis. With progress in antiviral therapies and prophylaxis protocols, the overall risk of clinically significant CMV disease has fallen sharply in solid organ transplant recipients (4). Thus, although CMV remains a threat—particularly in high-risk serostatus mismatches—appropriate prophylactic strategies appear just as effective in recipients with HCV D+/R– as in traditional cohorts.

Kidneys from donors who are HCV-viremic should remain a viable option, alleviating organ shortages, with lower than anticipated concern for CMV complications. Ongoing research is warranted, especially concerning longer-term infectious outcomes and specific subpopulations (such as high CMV risk serostatus mismatches). As the field continues to evolve, this study marks another critical stride toward evidence-based expansion of the transplant donor pool and moves patients closer to life-altering transplant.

Johnny Thornton, MBBS; Mary Kate Kelly, MB, BCh, BAO (Hons); and Sam Kant, MD, FASN, are with St. Vincent's University Hospital and University College Dublin, Ireland.

The authors report no conflicts of interest.

References

1. Potluri VS, et al. Risk of cytomegalovirus viremia following transplantation of hepatitis C-viremic donor kidneys into uninfected recipients: A multi-center retrospective cohort study. *Transpl Infect Dis* 2025; 27:e70011. doi: 10.1111/tid.70011
2. Daloul R, et al. Kidney transplant from hepatitis C viremic donors into aviremic recipients and risk for post-transplant BK and cytomegalovirus infection. *Transpl Infect Dis* 2022; 24:e13887. doi: 10.1111/tid.13887
3. Shah K, et al. Incidence of opportunistic viral infections in hepatitis C virus nucleic acid test negative recipients of kidneys from hepatitis C virus nucleic acid test positive donors. *Transpl Infect Dis* 2024; 26:e14364. doi: 10.1111/tid.14364
4. Durand CM, et al. Direct-acting antiviral prophylaxis in kidney transplantation from hepatitis C virus-infected donors to noninfected recipients: An open-label nonrandomized trial. *Ann Intern Med* 2018; 168:533–540. doi: 10.7326/M17-2871

Visit the ASN Communities Lounge at ASN Kidney Week

Exhibit Hall D, Booth 1525

Thursday, November 6

ASN Compensation Tool Demonstration — **10:00 — 10:30 a.m.**
Learn about the ASN Compensation Tool, powered by Phairify, and how to leverage this exclusive ASN member benefit. (Session 1)

General & Clinical Nephrology Poster Tour — **10:30 — 11:30 a.m.**
Led by Edgar Lerma, MD, FASN, and Roger Rodby, MD, FASN.

Becoming a Community Leader — **11:30 a.m. — 12:30 p.m.**
Engagement strategies, moderation, replies, and follow-through.

The Art of Discussion: Tips and Strategies — **12:30 — 1:30 p.m.**
Best practices, seed questions, and quality content.

Networking and Collaboration — **1:30 — 2:00 p.m.**
Leveraging connections, sharing stories, and team projects.

Friday, November 7

ASN Compensation Tool Demonstration — **10:00 — 11:30 a.m.**
Learn about the ASN Compensation Tool, powered by Phairify, and how to leverage this exclusive ASN member benefit. (Session 2)

Open Discussion — **10:30 — 11:00 a.m.**
New ideas, future directions, and lingering questions.

AI-Powered Kidney Care Network — **11:00 a.m. — 12:00 p.m.**
Engage with nephrology AI leaders, ask questions about the new ASN Community, and generate ideas for AI education and training.

Connect with the Kidney Health Initiative (KHI) — **12:00 — 1:00 p.m.**
KHI is ASN's public private partnership with the FDA and the broader kidney innovation community. Attend this informal gathering to network and learn how KHI advances patient-centered innovations in kidney health.

Forum for Trainees on Transplant Nephrology Training — **1:00 — 2:00 p.m.**
Are you a medical student, resident, or fellow interested in transplant nephrology? Learn what the joint ASN and American Society of Transplantation effort to secure ACGME accreditation for transplant nephrology means for you: briefing, questions-and-answers, and networking. Led by Roy D. Bloom, MD, MBChB, and Neeraj Singh, MD, MBA, FASN.

Saturday, November 8

Robert Califf: ASN President's Medal Recipient — **10:00 — 11:00 a.m.**
Meet-and-greet, questions-and-answers, and casual conversation.

Communities Library — **11:00 a.m. — 12:00 p.m.**
Keyword searching, studies and reports, and credible research.

Themed Communities — **12:00 — 1:00 p.m.**
Onco-nephrology, Women's Health & Research, Kidney Transplantation, and others.

Mentor Match Program — **1:00 — 2:00 p.m.**
Enrollment basics, search criteria, and building relationships.

ASN Communities

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

In the MIRROR trial, KRYSTEXXA with methotrexate:

DEMONSTRATED EFFICACY

71% (n=71/100) vs 39% (n=20/52) patient response* compared to KRYSTEXXA alone during Month 6 (*P*<0.0001)[1]

ESTABLISHED SAFETY PROFILE

4% (n=4/96) of patients experienced infusion reactions vs 31% (n=15/49) of patients treated with KRYSTEXXA alone

6-12 months of KRYSTEXXA may reverse years of urate deposition[1]

Best results were seen at 6-12 months.[1] Optimal treatment duration has not been established.[1] Individual results may vary.

KRYSTEXXA has not been studied to reverse damage to the kidneys, heart, or any of the body's organs.

*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]

The MIRROR RCT was a 52-week, randomized, double-blind, placebo-controlled trial conducted in adult patients with chronic gout refractory to conventional therapy to evaluate administration of KRYSTEXXA (8 mg Q2W) coadministered with 15 mg/week oral methotrexate and 1 mg/day oral folic acid (n=100) vs KRYSTEXXA with placebo (n=52).[1,2]

Q2W, once every 2 weeks; sUA, serum uric acid.

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.

KRYSTEXXA can dissolve years of systemic urate deposition[3,4]

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 JK, et al. *Arthritis Rheumatol.* 2023;75:293-304. **3.** Sundy JS, et al. *JAMA.* 2011;306:711-720. **4.** Dalbeth N, et al. *Joint Bone Spine.* 2024;91:105715.

AMGEN Rare Disease

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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From Kidneys to Cravings: Could GLP-1 Receptor Agonists Help Quench Thirst in Primary Polydipsia?

By Blaise Abramovitz and Helbert Rondon-Berrios

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Thirst is defined as the subjective sensation of needing or wanting to drink water. The primary physiologic triggers for thirst are plasma hypertonicity and a decreased effective arterial blood volume. Primary polydipsia (PP) refers to excessive water consumption in the absence of these physiologic stimuli. The main complications of PP include polyuria and recurrent, often severe, hyponatremia. The latter is associated with high rates of rehospitalization (1).

The kidneys typically defend against hyponatremia when large water loads are ingested by producing large volumes of dilute urine (2). However, this mechanism has its limits. The kidneys' capacity to excrete free water can be estimated using the following formula, where UOsm is urine osmolarity, OER is the osmolar excretion rate (the amount of solute excreted daily), and V is the daily urine volume: $\mathrm{UOsm} = \frac{\mathrm{OER}}{\mathrm{V}}$.

Rearranged, this gives: $\mathrm{V} = \frac{\mathrm{OER}}{\mathrm{UOsm}}$.

To estimate maximum urine output (Vmax) needed to protect against hyponatremia, we assume a maximal OER and a minimal UOsm. Under typical solute balance, OER corresponds to daily solute intake, which ranges from 600 to 900 mOsm/day. The minimum achievable UOsm (maximally diluted urine) is about 50 mOsm/L. Thus, $\mathrm{Vmax} = \frac{900\ \mathrm{mOsm/day}}{50\ \mathrm{mOsm/L}} = 18\ \mathrm{L/day}$.

This means that consuming more than 18 L of water per day can overwhelm the kidneys' ability to excrete water, resulting in hyponatremia. However, most patients with PP develop hyponatremia with fluid intakes just above 8 L/day (3). This discrepancy likely results from a concomitant defect in kidney electrolyte-free water excretion. Contributing factors include the use of psychotropic medications in this population—many of which are associated with the syndrome of inappropriate antidiuresis (SIAD) (1)—as well as intrinsic abnormalities in vasopressin sensitivity or a lowered osmotic threshold for arginine vasopressin secretion (reset osmostat) (4).

The underlying mechanism of excessive water drinking in PP remains poorly understood (4). Based on associated conditions, PP is broadly classified as either psychogenic or dipsogenic. Psychogenic polydipsia is commonly seen in patients with psychiatric disorders, especially schizophrenia spectrum disorders. These patients rarely report feeling thirsty and may describe delusional reasons for their water intake or report that drinking water reduces anxiety (4). Dipsogenic polydipsia occurs in individuals with hypothalamic lesions (e.g., from trauma, vascular, or infiltrative disease) that dysregulate thirst perception. It also occurs in individuals with habitual polydipsia who habitually drink excessive water, such as health enthusiasts and athletes, often due to the belief that water intake is inherently beneficial (5).

Despite its morbidity, treatment options for PP are often limited (5). However, emerging evidence suggests that glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) may offer a novel therapeutic option.

GLP-1 is a 30-amino acid peptide derived from the preproglucagon gene. After post-translational processing, GLP-1 is secreted by enteroendocrine L cells in the distal small intestine and colon in response to nutrient intake. Newly formed GLP-1 is released into the gut capillaries, acting hormonally, and also has local neuronal and paracrine effects due to its proximity to nerve endings and other cells in the gut (6). Most secreted GLP-1 is rapidly degraded: approximately 75% is inactivated by dipeptidyl peptidase-4 from microvilli capillary endothelial cells before reaching the portal vein, and about half of this is removed by the liver. Thus, only 10%–15% enters systemic circulation. Additionally, GLP-1 is synthesized in neurons of the brainstem, with projections to the hypothalamus and other regions involved in energy regulation and appetite control (6). GLP-1 exerts its effects by binding to GLP-1 receptors, which are widely expressed in the pancreas, gastrointestinal tract, brain, heart, and kidneys. In the pancreas, it stimulates insulin secretion and suppresses glucagon release. In the gastrointestinal tract, it delays gastric emptying, enhancing satiety and reducing food intake. In the brain, it activates satiety pathways via vagal afferent neurons and direct action on hypothalamic centers (6).

These effects have established GLP-1 RAs as a cornerstone in the management of type 2 diabetes and obesity. For nephrologists, they also represent one of the four key pillars in treating chronic kidney disease (7). Now, a new potential indication may be emerging on the horizon, as GLP-1 RAs have been shown to also reduce water intake.

The lamina terminalis, particularly its organum vasculosum and the subfornical organ, plays a key role in osmosensation and thirst regulation. These structures express GLP-1 receptors, and their deletion in animal models leads to polydipsia (8). Moreover, animal studies show that both peripheral and central administration of GLP-1 RAs significantly reduce water consumption, independently of their effects on food intake (9).

An initial study by Winzeler et al. investigated whether GLP-1 RAs reduce fluid intake in healthy individuals (10). This single-center, randomized, double-blind, placebo-controlled, 3-week crossover trial enrolled 20 healthy volunteers. Participants received either dulaglutide (1.5 mg) or placebo, administered subcutaneously once weekly for 3 weeks. The primary outcome—total fluid intake during an 8-hour evaluation visit—showed a trend toward significance in the dulaglutide group, with a median intake of 1300 mL compared with 1600 mL in the placebo group ($p = 0.06$). A secondary outcome, 24-hour urine output, was significantly lower with dulaglutide: median 1250 mL versus 1680 mL ($p = 0.04$). These findings laid the groundwork for a larger trial in patients with PP.

A subsequent randomized, double-blind, placebo-controlled, 3-week crossover trial enrolled 34 patients with PP (11). Participants received weekly subcutaneous injections of either dulaglutide (1.5 mg) or placebo. The primary outcome was total fluid intake during evaluation visits. Of the cohort, 41.2% were diagnosed with psychogenic polydipsia and 58.8% with habitual polydipsia. At baseline, median fluid intake was 4500 mL and was comparable across groups. Patients in the dulaglutide group showed a significant reduction in fluid intake—490 mL less than with placebo (95% confidence interval [CI], –780 to –199; $p = 0.002$). During treatment, the median fluid intake was 2460 mL (95% CI, 1946–2475) with dulaglutide versus 2950 mL (95% CI, 2435–3465) with placebo, representing a relative reduction of 17%. A secondary outcome, 24- hour urine output, was also significantly lower with dulaglutide: 3591 mL compared with 4534 mL with placebo, with a mean difference of –943 mL (95% CI, –1473 to –413; $p = 0.001$). Thirst perception, assessed using the Numeric Rating Scale, was lower in the dulaglutide group both during the evaluation visit and during a thirst-craving task conducted in a functional magnetic resonance imaging session. Interestingly, no corresponding changes in brain activity were detected on functional imaging. A notable adverse event was mild hyponatremia in two participants. In one patient, the lowest plasma sodium levels were 133 mmol/L with dulaglutide and 131 mmol/L with placebo; in the other, levels were 132 mmol/L with dulaglutide and 133 mmol/L with placebo. Both individuals had severe polydipsia at baseline, with urine outputs exceeding 6 L/day.

These findings highlight dulaglutide as a potentially valuable therapeutic agent for PP, a condition with limited treatment options. However, some key questions remain. Is this a class effect? Notably, dulaglutide is a relatively large GLP-1 RA (>50–60 kDa), which may limit its ability to cross the blood–brain barrier (12). Is it possible that smaller GLP-1 RAs, such as liraglutide or semaglutide, could exert more potent or central effects? Additionally, could GLP-1 RAs serve as adjunctive therapy to reduce fluid intake in other hyponatremic disorders, such as SIAD? Further research is warranted to explore these possibilities. ■

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The authors report no conflicts of interest.

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CREATIVE CORTEX

The Haunted Nephron

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A spectral ballet of form and function, this artwork in honor of Halloween embodies the eerie yet vital essence of life's filtration. The glomerulus, twisted like autumn's whispers, pulses in spectral hues of orange and green, mimicking the pumpkin's harvest heart. Blood flow spirals into surreal tendrils, dissolving into an otherworldly mist. This piece is a haunting reminder of nature's cycles—of filtration, renewal, and the silent mysteries that keep life's symphony playing in the shadows. ■

Artwork by AnilzArt. Anil Saxena, MD, FASN, is a digital artist based in Dubai, United Arab Emirates. His abstract artwork blends trained medical expertise with vibrant color palettes, creating visually captivating landscapes of human identity and transformation. Saxena's work has been exhibited internationally and featured on the covers of medical journals.

INDICATIONS & USAGE

FILSPARI® (sparsentan) is indicated to slow kidney function decline in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk for disease progression.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: HEPATOTOXICITY AND EMBRYO-FETAL TOXICITY

Because of the risk of hepatotoxicity, FILSPARI is available only through a restricted program called the FILSPARI REMS. Under the FILSPARI REMS, prescribers, patients and pharmacies must enroll in the program.

Hepatotoxicity

Some Endothelin Receptor Antagonists (ERAs) have caused elevations of aminotransferases, hepatotoxicity, and liver failure. In clinical studies, elevations in aminotransferases (ALT or AST) of at least 3-times the Upper Limit of Normal (ULN) have been observed in up to 3.5% of FILSPARI-treated patients, including cases confirmed with rechallenge.

Measure transaminases and bilirubin before initiating treatment and then every 3 months during treatment. Interrupt treatment and closely monitor patients who develop aminotransferase elevations more than 3x ULN.

FILSPARI should generally be avoided in patients with elevated aminotransferases (>3x ULN) at baseline because monitoring for hepatotoxicity may be more difficult and these patients may be at increased risk for serious hepatotoxicity.

Embryo-Fetal Toxicity

FILSPARI is contraindicated for use during pregnancy because it may cause fetal harm if used by pregnant patients. Therefore, in patients who can become pregnant, exclude pregnancy prior to initiation of FILSPARI. Advise use of effective contraception before the initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI. When pregnancy is detected, discontinue FILSPARI as soon as possible.

Contraindications

FILSPARI is contraindicated in patients who are pregnant. Do not coadminister FILSPARI with angiotensin receptor blockers (ARBs), ERAs, or aliskiren.

Warnings and Precautions

- **Hepatotoxicity:** Elevations in ALT or AST of at least 3-fold ULN have been observed in up to 3.5% of FILSPARI-treated patients, including cases confirmed with rechallenge. While no concurrent elevations in bilirubin >2-times ULN or cases of liver failure were observed in FILSPARI-treated patients in clinical trials, some ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. To reduce the risk of potential serious hepatotoxicity, measure serum aminotransferase levels and total bilirubin prior to initiation of treatment and then every 3 months during treatment.

  Advise patients with symptoms suggesting hepatotoxicity (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching) to immediately stop treatment with FILSPARI and seek medical attention. If aminotransferase levels are abnormal at any time during treatment, interrupt FILSPARI and monitor as recommended.

  Consider re-initiation of FILSPARI only when hepatic enzyme levels and bilirubin return to pretreatment values and only in patients who have not experienced clinical symptoms of hepatotoxicity. Avoid initiation of FILSPARI in patients with elevated aminotransferases (>3x ULN) because monitoring hepatotoxicity in these patients may be more difficult and these patients may be at increased risk for serious hepatotoxicity.
- **FILSPARI REMS:** Due to the risk of hepatotoxicity, FILSPARI is available only through a restricted program called the FILSPARI REMS. Prescribers, patients, and pharmacies must be enrolled in the REMS program and comply with all requirements (www.filsparirems.com).
- **Embryo-Fetal Toxicity:** Based on data from animal reproduction studies, FILSPARI may cause fetal harm when administered to a pregnant patient and is contraindicated during pregnancy. The available human data for ERAs do not establish the presence or absence of fetal harm related to the use of FILSPARI. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy before initiating treatment with FILSPARI. Advise patients who can become pregnant to use effective contraception prior to initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI. When pregnancy is detected, discontinue FILSPARI as soon as possible.
- **Hypotension:** Hypotension has been observed in patients treated with ARBs and ERAs. There was a greater incidence of hypotension-associated adverse events, some serious, including dizziness, in patients treated with FILSPARI compared to irbesartan. In patients at risk for hypotension, consider eliminating or adjusting other antihypertensive medications and maintaining appropriate volume status. If hypotension develops, despite elimination or reduction of other antihypertensive medications, consider a dose reduction or dose interruption of FILSPARI. A transient hypotensive response is not a contraindication to further dosing of FILSPARI, which can be given once blood pressure has stabilized.
- **Acute Kidney Injury:** Monitor kidney function periodically. Drugs that inhibit the renin-angiotensin system (RAS) can cause kidney injury. Patients whose kidney function may depend in part on the activity of the RAS (e.g., patients with renal artery stenosis, chronic kidney disease, severe congestive heart failure, or volume depletion) may be at particular risk of developing acute kidney injury on FILSPARI. Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in kidney function while on FILSPARI.
- **Hyperkalemia:** Monitor serum potassium periodically and treat appropriately. Patients with advanced kidney disease, taking concomitant potassium-increasing drugs (e.g., potassium supplements, potassium-sparing diuretics), or using potassium-containing salt substitutes are at increased risk for developing hyperkalemia. Dosage reduction or discontinuation of FILSPARI may be required.
- **Fluid Retention:** Fluid retention may occur with ERAs, and has been observed in clinical studies with FILSPARI. FILSPARI has not been evaluated in patients with heart failure. If clinically significant fluid retention develops, evaluate the patient to determine the cause and the potential need to initiate or modify the dose of diuretic treatment then consider modifying the dose of FILSPARI.

Most common adverse reactions

The most common adverse reactions (≥5%) are hyperkalemia, hypotension (including orthostatic hypotension), peripheral edema, dizziness, anemia, and acute kidney injury.

Drug interactions

- **Renin-Angiotensin System (RAS) Inhibitors and ERAs:** Do not coadminister FILSPARI with ARBs, ERAs, or aliskiren due to increased risks of hypotension, syncope, hyperkalemia, and changes in renal function (including acute renal failure).
- **Strong and Moderate CYP3A Inhibitors:** Avoid concomitant use of FILSPARI with strong CYP3A inhibitors. If a strong CYP3A inhibitor cannot be avoided, interrupt FILSPARI treatment. When resuming treatment with FILSPARI, consider dose titration. Monitor blood pressure, serum potassium, edema, and kidney function regularly when used concomitantly with moderate CYP3A inhibitors. Concomitant use with a strong CYP3A inhibitor increases sparsentan exposure which may increase the risk of FILSPARI adverse reactions.
- **Strong CYP3A Inducers:** Avoid concomitant use with a strong CYP3A inducer. Concomitant use with a strong CYP3A inducer decreases sparsentan exposure which may reduce FILSPARI efficacy.
- **Antacids and Acid Reducing Agents:** Administer FILSPARI 2 hours before or after administration of antacids. Avoid concomitant use of acid reducing agents (histamine H2 receptor antagonist and PPI proton pump inhibitor) with FILSPARI. Sparsentan exhibits pH-dependent solubility. Antacids or acid reducing agents may decrease sparsentan exposure which may reduce FILSPARI efficacy.

FILSPARI® (sparsentan) tablets 200 mg/400 mg

FOR ADULTS WITH IgA NEPHROPATHY

UPDATE: Simplified FILSPARI® REMS Program

Reduced REMS testing requirements for treating your adult IgAN patients with FILSPARI[1]

Liver function testing every 3 months from the start[1]

Measure transaminases and bilirubin **before initiating** treatment with FILSPARI

No REMS requirement for pregnancy testing[1]

Exclude pregnancy before initiation of treatment. Advise **use of effective contraception** prior to initiation, during, and for 2 weeks after treatment discontinuation; **discontinue** FILSPARI if patient becomes pregnant

Get your patients started today

Scan or visit **FILSPARIhcp.com** to learn how

IgAN=immunoglobulin A nephropathy; REMS=Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION: Drug interactions (cont'd)

- **Non-Steroidal Anti-Inflammatory Agents (NSAIDs), Including Selective Cyclooxygenase-2 (COX-2) Inhibitors:** Monitor for signs of worsening renal function with concomitant use with NSAIDs (including selective COX-2 inhibitors). In patients with volume depletion (including those on diuretic therapy) or with impaired kidney function, concomitant use of NSAIDs (including selective COX-2 inhibitors) with drugs that antagonize the angiotensin II receptor may result in deterioration of kidney function, including possible kidney failure.
- **CYP2B6, 2C9, and 2C19 Substrates:** Monitor for efficacy of concurrently administered CYP2B6, 2C9, and 2C19 substrates and consider dosage adjustment in accordance with the Prescribing Information. Sparsentan decreases exposure of these substrates, which may reduce efficacy related to these substrates.
- **P-gp and BCRP Substrates:** Avoid concomitant use of sensitive substrates of P-gp and BCRP with FILSPARI. Sparsentan may increase exposure of these transporter substrates which may increase the risk of adverse reactions related to these substrates.
- **Agents Increasing Serum Potassium:** Monitor serum potassium frequently in patients treated with FILSPARI and other agents that increase serum potassium. Concomitant use of FILSPARI with potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, or other drugs that raise serum potassium levels may result in hyperkalemia.

For additional Important Safety Information, please see the Brief Summary of the full Prescribing Information on the following pages, including BOXED WARNING.

Reference: 1. FILSPARI Prescribing Information. San Diego, CA: Travere Therapeutics, Inc.

TRAVERE® THERAPEUTICS

Brief Summary of full Prescribing Information for FILSPARI® (sparsentan) tablets, for oral use

Initial U.S. Approval: 2023

INDICATIONS AND USAGE

FILSPARI is indicated to slow kidney function decline in adults with primary immunoglobulin A nephropathy (IgAN) who are at risk for disease progression.

WARNING: HEPATOTOXICITY and EMBRYO-FETAL TOXICITY

Because of the risk of hepatotoxicity, FILSPARI is available only through a restricted program called the FILSPARI REMS. Under the FILSPARI REMS, prescribers, patients, and pharmacies must enroll in the program.

Hepatotoxicity

Some Endothelin Receptor Antagonists (ERAs) have caused elevations of aminotransferases, hepatotoxicity, and liver failure. In clinical studies, elevations in aminotransferases (ALT or AST) of at least 3-times the Upper Limit of Normal (ULN) have been observed in up to 3.5% of FILSPARI-treated patients, including cases confirmed with rechallenge.

Measure transaminases and bilirubin before initiating treatment and then every 3 months during treatment. Interrupt treatment and closely monitor patients who develop aminotransferase elevations more than 3-times ULN.

FILSPARI should generally be avoided in patients with elevated aminotransferases (>3-times ULN) at baseline because monitoring for hepatotoxicity may be more difficult and these patients may be at increased risk for serious hepatotoxicity.

Embryo-Fetal Toxicity

FILSPARI is contraindicated for use during pregnancy because it may cause fetal harm if used by pregnant patients. Therefore, in patients who can become pregnant, exclude pregnancy prior to initiation of FILSPARI. Advise use of effective contraception before the initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI. When pregnancy is detected, discontinue FILSPARI as soon as possible.

CONTRAINDICATIONS

Use of FILSPARI is contraindicated in patients who are pregnant.

Do not coadminister FILSPARI with angiotensin receptor blockers (ARBs), ERAs, or aliskiren.

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Elevations in ALT or AST of at least 3-fold ULN have been observed in up to 3.5% of FILSPARI-treated patients, including cases confirmed with rechallenge. While no concurrent elevations in bilirubin greater than 2-times ULN or cases of liver failure were observed in FILSPARI-treated patients in clinical trials, some endothelin receptor antagonists have caused elevations of aminotransferases, hepatotoxicity, and liver failure. To reduce the risk of potential serious hepatotoxicity, measure serum aminotransferase levels and total bilirubin prior to initiation of treatment and then every 3 months during treatment.

Advise patients with symptoms suggesting hepatotoxicity (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching) to immediately stop treatment with FILSPARI and seek medical attention. If aminotransferase levels are abnormal at any time during treatment, interrupt FILSPARI and monitor as recommended.

Consider re-initiation of FILSPARI only when hepatic enzyme levels and bilirubin return to pretreatment values and only in patients who have not experienced clinical symptoms of hepatotoxicity.

Avoid initiation of FILSPARI in patients with elevated aminotransferases (greater than 3-times ULN) because monitoring hepatotoxicity in these patients may be more difficult and these patients may be at increased risk for serious hepatotoxicity.

FILSPARI REMS

For all patients, FILSPARI is available only through a restricted program under a REMS called the FILSPARI REMS because of the risk of hepatotoxicity.

Important requirements of the FILSPARI REMS include the following:

- Prescribers must be certified with the FILSPARI REMS by enrolling and completing training.
- All patients must enroll in the FILSPARI REMS prior to initiating treatment and comply with monitoring requirements.
- Pharmacies that dispense FILSPARI must be certified with the FILSPARI REMS and must dispense only to patients who are authorized to receive FILSPARI.

Further information is available at www.filsparirems.com or 1-833-513-1325.

Embryo-Fetal Toxicity

Based on data from animal reproduction studies, FILSPARI may cause fetal harm when administered to a pregnant patient and is contraindicated for use during pregnancy. The available human data for ERAs do not establish the presence or absence of fetal harm related to the use of FILSPARI. Counsel patients who can become pregnant of the potential risk to a fetus. Exclude pregnancy before initiating treatment with FILSPARI. Advise patients who can become pregnant to use effective contraception prior to initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI. When pregnancy is detected, discontinue FILSPARI as soon as possible.

Hypotension

Hypotension has been observed in patients treated with ARBs and endothelin receptor antagonists (ERAs) and was observed in clinical studies with FILSPARI. In the PROTECT trial, there was a greater incidence of hypotension-associated adverse events, some serious, including dizziness, in patients treated with FILSPARI compared to irbesartan.

In patients at risk for hypotension, consider eliminating or adjusting other antihypertensive medications and maintaining appropriate volume status.

If hypotension develops, despite elimination or reduction of other antihypertensive medications, consider a dose reduction or dose interruption of FILSPARI. A transient hypotensive response is not a contraindication to further dosing of FILSPARI, which can be given once blood pressure has stabilized.

Acute Kidney Injury

Monitor kidney function periodically. Drugs that inhibit the renin-angiotensin system can cause acute kidney injury. Patients whose kidney function may depend in part on the activity of the renin-angiotensin system (e.g., patients with renal artery stenosis, chronic kidney disease, severe congestive heart failure, or volume depletion) may be at particular risk of developing acute kidney injury on FILSPARI. Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in kidney function while on FILSPARI.

Hyperkalemia

Monitor serum potassium periodically and treat appropriately. Patients with advanced kidney disease or taking concomitant potassium-increasing drugs (e.g., potassium supplements, potassium-sparing diuretics), or using potassium-containing salt substitutes are at increased risk for developing hyperkalemia. Dosage reduction or discontinuation of FILSPARI may be required.

Fluid Retention

Fluid retention may occur with endothelin receptor antagonists and has been observed in clinical studies with FILSPARI. FILSPARI has not been evaluated in patients with heart failure.

If clinically significant fluid retention develops, evaluate the patient to determine the cause and the potential need to initiate or modify the dose of diuretic treatment then consider modifying the dose of FILSPARI.

ADVERSE REACTIONS

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 FILSPARI was evaluated in PROTECT (NCT03762850), a randomized, double-blind, active-controlled clinical study in adults with IgAN.

The data below reflect FILSPARI exposure in 202 patients with a median duration of 110 weeks.

The most common adverse reactions are presented in the table below.

Adverse Reactions Reported in 2% or More of Subjects Treated with FILSPARI

	FILSPARI (N=202) n (%)	**Irbesartan (N=202) n (%)**
Hyperkalemia[1]	34 (17)	27 (13)
Hypotension (including orthostatic hypotension)	33 (16)	13 (6)
Peripheral edema[1]	33 (16)	29 (14)
Dizziness[1]	32 (16)	14 (7)
Anemia	16 (8)	9 (4)
Acute kidney injury	12 (6)	5 (2)
Transaminase elevations[2]	7 (3.5)	8 (4.0)

[1] Includes related terms.

[2] Elevations in ALT or AST greater than 3-fold ULN.

Laboratory Tests

Initiation of FILSPARI may cause an initial small decrease in estimated glomerular filtration rate (eGFR) that occurs within the first 4 weeks of starting therapy and then stabilizes.

The incidence of a hemoglobin decrease >2 g/dL compared to baseline and below the lower limit of normal was greater for the FILSPARI arm (19%) compared to the irbesartan arm (13%). This decrease is thought to be in part due to hemodilution. There were no treatment discontinuations due to anemia or hemoglobin decrease in the PROTECT study.

DRUG INTERACTIONS

Renin-Angiotensin System (RAS) Inhibitors and ERAs

Do not coadminister FILSPARI with ARBs, ERAs, or aliskiren.

Combined use of these agents is associated with increased risks of hypotension, syncope, hyperkalemia, and changes in renal function (including acute renal failure).

Strong and Moderate CYP3A Inhibitors

Avoid concomitant use of FILSPARI with strong CYP3A inhibitors. If a strong CYP3A inhibitor cannot be avoided, interrupt treatment with FILSPARI. When resuming treatment with FILSPARI, consider dose titration.

Monitor blood pressure, serum potassium, edema, and kidney function regularly when used concomitantly with moderate CYP3A inhibitors. No FILSPARI dose adjustment is needed.

Sparsentan is a CYP3A substrate. Concomitant use with a strong CYP3A inhibitor increases sparsentan C_{max} and AUC, which may increase the risk of FILSPARI adverse reactions.

Strong CYP3A Inducers

Avoid concomitant use with a strong CYP3A inducer. Sparsentan is a CYP3A substrate. Concomitant use with a strong CYP3A inducer decreases sparsentan C_{max} and AUC, which may reduce FILSPARI efficacy.

Antacids and Acid Reducing Agents

Administer FILSPARI 2 hours before or after administration of antacids. Avoid concomitant use of acid reducing agents (histamine H2 receptor antagonist and PPI proton pump inhibitor) with FILSPARI. Sparsentan exhibits pH-dependent solubility. Antacids or acid reducing agents may decrease sparsentan exposure which may reduce FILSPARI efficacy.

Non-Steroidal Anti-Inflammatory Agents (NSAIDs), Including Selective Cyclooxygenase-2 (COX-2) Inhibitors

Monitor for signs of worsening renal function with concomitant use with NSAIDs (including selective COX-2 inhibitors). In patients with volume depletion (including those on diuretic therapy) or with impaired kidney function, concomitant use of NSAIDs (including selective COX-2 inhibitors) with drugs that antagonize the angiotensin II receptor may result in deterioration of kidney function, including possible kidney failure. These effects are usually reversible.

CYP2B6, 2C9, and 2C19 Substrates

Monitor for efficacy of the concurrently administered CYP2B6, 2C9, and 2C19 substrates and consider dosage adjustment in accordance with the Prescribing Information. Sparsentan is an inducer of CYP2B6, 2C9, and 2C19. Sparsentan decreases exposure of these substrates, which may reduce efficacy related to these substrates.

P-gp and BCRP Substrates

Avoid concomitant use of sensitive substrates of P-gp and BCRP with FILSPARI. Sparsentan is an inhibitor of P-gp and BCRP. Sparsentan may increase exposure of these transporter substrates, which may increase the risk of adverse reactions related to these substrates.

Agents Increasing Serum Potassium

Monitor serum potassium frequently in patients treated with FILSPARI and other agents that increase serum potassium. Concomitant use of FILSPARI with potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, or other drugs that raise serum potassium levels may result in hyperkalemia.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on data from animal reproductive toxicity studies, FILSPARI may cause fetal harm, including birth defects and fetal death, when administered to a pregnant patient and is contraindicated during pregnancy. Available data from reports of pregnancy in clinical trials with FILSPARI are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Available data from postmarketing reports and published literature over decades of use with ERA in the same class as FILSPARI have not identified an increased risk of fetal harm; however, these data are limited. Methodological limitations of these postmarketing reports and published literature include lack of a control group; limited information regarding dose, duration, and timing of drug exposure; and missing data. These limitations preclude establishing a reliable estimate of the risk of adverse fetal and neonatal outcomes with maternal ERA use. In animal reproduction studies, oral administration of sparsentan to pregnant rats throughout organogenesis at 10-times the maximum recommended human dose (MRHD) in mg/day caused teratogenic effects in rats, including craniofacial malformations, skeletal abnormalities, increased embryo-fetal lethality, and reduced fetal weights. Advise pregnant patients of the potential risk to the fetus.

Lactation

Risk Summary

There are no data on the presence of sparsentan in human milk, the effects on the breastfed infant, or the effect on milk production. Because of the potential for adverse reactions, such as hypotension in breastfed infants, advise patients not to breastfeed during treatment with FILSPARI.

Females and Males of Reproductive Potential

Based on data from animal reproductive toxicity studies, FILSPARI may cause fetal harm, including birth defects and fetal death, when administered to a pregnant patient and is contraindicated during pregnancy.

Pregnancy Testing

Exclude pregnancy before initiating FILSPARI in females of reproductive potential. The patient should contact their physician immediately for pregnancy testing if onset of menses is delayed or pregnancy is suspected. If the pregnancy test is positive, the physician and patient should discuss the risks to their pregnancy and the fetus.

Contraception

Patients who can become pregnant who are using FILSPARI must use an effective method of contraception prior to initiation of treatment, during treatment, and for two weeks after discontinuation of treatment with FILSPARI to prevent pregnancy.

Pediatric Use

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

Geriatric Use

Of the total number of subjects in the PROTECT study of FILSPARI, 15 (7.4%) were 65 and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

Hepatic Impairment

Avoid use of FILSPARI in patients with any hepatic impairment (Child-Pugh class A-C) because of the potential risk of serious liver injury.

OVERDOSAGE

There is no experience with overdose with FILSPARI. Sparsentan has been given in doses up to 1600 mg/day in healthy volunteers, or up to 400 mg/day in IgAN patients. Overdose of FILSPARI may result in decreased blood pressure. In the event of an overdose, standard supportive measures should be taken, as required. Dialysis is unlikely to be effective because sparsentan is highly protein-bound.

This information is not comprehensive. Visit FILSPARIhcp.com or call 1-877-659-5518 to obtain the full Prescribing Information.

Distributed by: Travere Therapeutics, Inc., San Diego, CA 92130

TRAVERE® THERAPEUTICS

No Cardiovascular Benefit of Spironolactone in Patients on Dialysis

https://doi.org/10.62716/kn.002142025

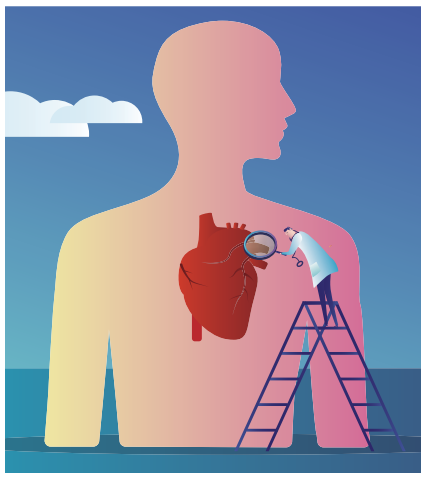
The aldosterone blocker spironolactone does not reduce adverse cardiovascular outcomes in patients on maintenance dialysis, according to a clinical trial report in *The Lancet*.

The ACHIEVE trial enrolled adult patients receiving maintenance hemodialysis for kidney failure. Patients were drawn from 143 dialysis centers in 12 countries, ranging from lower-middle to high-income countries. Patients who tolerated oral spironolactone (25 mg/day) during a 7-week, open-label run-in period were randomly assigned to continued spironolactone treatment or placebo. Groups were compared on a primary composite outcome of death from cardiovascular causes or hospitalization for heart failure.

A total of 3565 patients (mean age, 61 years) were randomized. Among the patients, 63% were men, and the primary cause of kidney failure was diabetic nephropathy in 43%.

After a planned interim analysis of 75% of expected primary outcome events, the study was halted early due to futility. At a median follow-up of 1.8 years, a primary outcome event occurred in 258 patients assigned to spironolactone and in 276 in the placebo group. Incidence of the composite outcome was 10.46 and 11.33 events per 100 patient-years, respectively.

The two groups had similar incidence rates for both cardiovascular mortality and all-cause hospitalization. Patients assigned to



spironolactone had a higher rate of severe hyperkalemia: 4.97 versus 3.23 per 100 patient-years.

Previous studies have suggested that mineralocorticoid receptor antagonist therapy might lower the high risk of cardiovascular death among patients on dialysis. However, the ACHIEVE trial finds no significant reduction in cardiovascular mortality or heart failure hospitalization in patients assigned to spironolactone compared with placebo.

"Future research should consider alternatives to steroidal mineralocorticoid receptor antagonism to reduce cardiovascular morbidity and mortality in patients receiving maintenance haemodialysis," the researchers conclude. They call for further efforts to reconcile the ACHIEVE findings with a previous meta-analysis suggesting large mortality benefits with mineralocorticoid receptor antagonists [Walsh M, et al.; ACHIEVE Investigators. Spironolactone versus placebo in patients undergoing maintenance dialysis (ACHIEVE): An international, parallel-group, randomised controlled trial. *Lancet* 2025; 406:695–704. doi: 10.1016/S0140-6736(25)01198-5].

Noninvasive Marker of Rejection in Pediatric Kidney Transplant Recipients?

https://doi.org/10.62716/kn.002152025

Donor-derived cell-free DNA (dd-cfDNA) may provide a useful noninvasive marker of rejection in pediatric kidney allograft recipients, reports a study in *Transplantation*.

The study included an unselected group of 196 pediatric transplant recipients, drawn from one US and one French transplant center. The patients underwent a total of 367 biopsies with concomitant dd-cfDNA assessment. The median age was 12 years at transplant and 15 years at the time of allograft biopsy and dd-cfDNA measurement. Levels of dd-cfDNA were analyzed for association with biopsy histologic findings and for detection of allograft rejection.

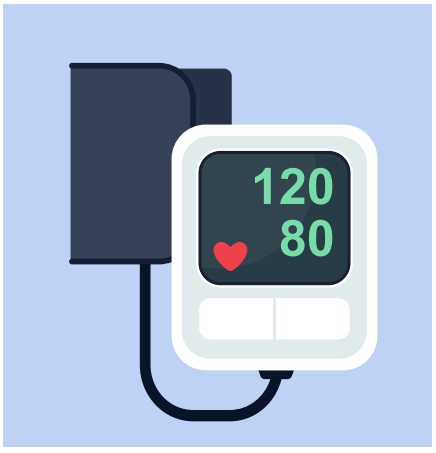
Higher plasma dd-cfDNA levels were associated with higher degrees of biopsy-detected inflammation, both interstitial and microvascular. Levels of dd-cfDNA were also associated with severity of interstitial

fibrosis and tubular atrophy, although not with other chronic allograft lesions.

dd-cfDNA was "strongly and independently" associated with allograft rejection: odds ratio, 1.89. On analysis of different detection strategies, discrimination was 0.76 with dd-cfDNA alone. When dd-cfDNA was added to standard of care, discrimination increased from 0.80 to 0.84.

Allograft rejection is the main cause of graft loss after pediatric kidney transplant. Current strategies based on measurement of functional markers and detection of donor-specific antibodies lack sensitivity and specificity in detecting biopsy-confirmed rejection. dd-cfDNA has been proposed as a potential noninvasive biomarker for early detection of allograft rejection.

The new findings "confirm that dd-cfDNA is strongly associated with the presence of allograft rejection in pediatric kidney transplant recipients," the researchers conclude. The association is independent of clinical, biologic, and immunologic factors and improves detection of rejection when combined with current standard of care. The authors highlight the need for "further specific studies...to better define how to use this promising biomarker in various contexts of use in children" [Hogan J, et al. Donor-derived cell-free DNA as a noninvasive biomarker of kidney allograft rejection in pediatric kidney transplantation. *Transplantation* 2025; 109:1520–1525. doi: 10.1097/TP.0000000000005403].



Baxdrostat Lowers Systolic BP in Hard-to-Control Hypertension

https://doi.org/10.62716/kn.002132025

The investigational aldosterone-lowering drug baxdrostat reduces systolic blood pressure in patients with uncontrolled or resistant hypertension, reports a phase 3 clinical trial in *The New England Journal of Medicine*.

The randomized, double-blind "BaxHTN" trial included 794 adults with hard-to-control hypertension, defined as seated systolic blood pressure between 140 and 170 mm Hg. All had continued high blood pressure despite treatment with two (uncontrolled hypertension) or three or more (resistant hypertension) antihypertensive medications, including a diuretic.

After a 2-week, open-label run-in period, patients whose seated systolic blood pressure remained at 135 mm Hg or higher were assigned to continued treatment with baxdrostat (1 or 2 mg) or placebo. The change in seated systolic blood pressure from baseline through the 12-week treatment period was assessed.

Baxdrostat was associated with greater reductions in seated systolic blood pressure: by 14.5 mm Hg in the 1-mg dose group and by 15.7 mm Hg in the 2-mg group compared with 5.8 mm Hg in those with placebo. Placebo-corrected differences were –8.7 and –9.8 mm Hg, respectively.

Patients assigned to baxdrostat were more likely to have potassium levels exceeding 6.0 mmol/L: 2.3% in the 1-mg dose group and 3.0% in the 2-mg group compared with 0.4% with placebo. In a randomized withdrawal period, findings suggested "a slow offset of the effect of baxdrostat on blood pressure…consistent with its mechanism of action on sodium homeostasis."

Aldosterone dysregulation is thought to be a key contributor to hard-to-control hypertension. Baxdrostat, a highly selective direct aldosterone inhibitor, has shown promise as a once-daily treatment for uncontrolled or resistant hypertension.

The new study shows reductions in seated systolic blood pressure with baxdrostat, added to background therapy for uncontrolled or resistant hypertension. Findings suggest "an important role for dysregulated aldosterone in the pathophysiology of both uncontrolled and resistant hypertension, along with a potentially broader population of patients with hypertension," the researchers write [Flack JM, et al.; BaxHTN Investigators. Efficacy and safety of baxdrostat in uncontrolled and resistant hypertension. *N Engl J Med*, published online August 30, 2025. doi: 10.1056/NEJMoa2507109].

"Steady Increase" in Kidney Failure With Replacement Therapy Worldwide

https://doi.org/10.62716/kn.001912025

The global burden of kidney failure with replacement therapy (KFRT) has increased steadily over the past 3 decades, with wide geographic variations in incidence and treatment availability, according to a systematic analysis, published in *The Lancet Global Health*.

The researchers analyzed worldwide kidney registry data on KFRT, defined as being on dialysis for 90 days or longer or undergoing a kidney transplant. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) modeling framework was used to estimate the prevalence and etiologies of KFRT by age and sex from 1990 to 2023. The analysis included data from 204 countries and territories, seven super-regions, and 21 regions.

Findings suggest "a steady increase in KFRT prevalence" over the study period. In 2023, there were 4.6 million cases of KFRT worldwide, with an age-standardized prevalence of 50.7 per 100,000 population. Prevalence was highest in the GBD high-income super-region (111.0 per 100,000) and was lowest in sub-Saharan Africa (3.8 per 100,000). Within North America, 2023 prevalence was 176.0 per 100,000 in the United States versus 75.2 per 100,000 in Canada.

The data found 3.6 million dialysis cases in 2023: age-standardized prevalence, 39.3 per 100,000. For kidney transplant, age-standardized prevalence was 11.3 per 100,000—52.1 per 100,000 in high-income North America versus 0.2 per 100,000 in western sub-Saharan Africa. In nearly every country, dialysis and transplantation prevalence rates were higher in males compared with females.

Type 2 diabetes and hypertension were the most common etiologies. These two causes accounted for 40.6% of global KFRT cases in 2023 and showed the greatest increases over the study period.

Although previous GBD analyses have reported estimates of chronic kidney disease (CKD), the new report is the first, to our knowledge, to focus on the global burden of KFRT. Along with the steady increases in KFRT over the past 3 decades, the findings highlight "large and stark [geographic] disparities."

The regional differences likely reflect "systemic issues such as inadequate [health care] infrastructure, insufficient awareness, and barriers to timely intervention for treatment," the researchers write. They conclude: "As health systems work to expand their KFRT capacity and address the weaknesses, incorporating CKD prevention into both new and existing [noncommunicable] disease policies could provide a cost-effective solution" [GBD 2023 Kidney Failure with Replacement Therapy Collaborators. Global, regional, and national prevalence of kidney failure with replacement therapy and associated aetiologies, 1990–2023: A systematic analysis for the Global Burden of Disease Study 2023. *Lancet Glob Health* 2025; 13:e1378–1395. doi: 10.1016/S2214-109X(25)00198-6].

Trial Supports Canagliflozin for Type 2 Diabetes in Children and Adolescents

https://doi.org/10.62716/kn.001932025

The sodium-glucose cotransporter-2 inhibitor canagliflozin is safe and effective in lowering hemoglobin A_{1c} (HbA_{1c}) in children and adolescents with type 2 diabetes mellitus (T2DM), reports a clinical trial in the *Annals of Internal Medicine*.

The randomized phase 3 trial included 171 children and adolescents (aged ≥10 to <18 years) with T2DM and an HbA_{1c} of 6.5% or less, enrolled at 104 sites in 10 countries. Patients were randomly assigned to once-daily treatment with canagliflozin (10 mg) or placebo. After 12 weeks, those with HbA_{1c} of 7.0% or greater and an estimated glomerular filtration rate (eGFR) of 60 mL/min/1.73 m^2 were rerandomized to continue canagliflozin at 100 mg or placebo or to increase to canagliflozin to 300 mg or placebo.

Study treatment continued for 52 weeks. The primary efficacy outcome was the change in HbA_{1c} from baseline to 26 weeks. Secondary efficacy outcomes and adverse events were analyzed up to 52 weeks.

Mean HbA_{1c} decreased from 7.8% at baseline to 7.3% at 26 weeks in patients assigned to canagliflozin compared with

an increase from 8.3% to 8.6% with placebo. The least-squares mean difference was –0.8% in favor of canagliflozin. The benefit was similar in the subgroup of patients who continued on background metformin treatment, with or without insulin.

Patients receiving canagliflozin compared with placebo were more likely to reach an HbA_{1c} target of under 6.5%: 36.3% versus 14.0%. Canagliflozin was associated with greater improvement in fasting plasma glucose and body weight.

Treatment-emergent adverse events were similar to those reported in adults. Serious adverse events occurred in 9.5% of the canagliflozin group and 5.7% of the placebo group; only one of these events (inadequate diabetes control in a patient assigned to placebo) was considered related to study medication. Symptomatic hypoglycemia occurred in 11.9% of the canagliflozin group versus 10.3% with placebo. No patient had a decline in eGFR to less than 60 mL/min/1.73 m^2.

Amid dramatic increases in the incidence of T2DM in children and adolescents, treatment options are limited. Canagliflozin is approved for treatment of T2DM in adults, but its safety and efficacy in pediatric patients has been unclear.

This placebo-controlled trial shows improved glycemic control with canagliflozin in children and adolescents with inadequately controlled T2DM. The safety profile appears similar to that in adults. The findings "provide support for the use of canagliflozin in the clinical management of T2DM in children and adolescents aged 10 years or older," the investigators conclude [Nadgir U, et al. Treatment with canagliflozin versus placebo in children and adolescents with type 2 diabetes: A randomized clinical trial. *Ann Intern Med* 2025; 78:1217–1226. doi: 10.7326/ANNALS-24-04017]. ■

C-Reactive Protein Associated With Kidney Outcomes in Atherosclerotic CVD

https://doi.org/10.62716/kn.002122025

Patients with atherosclerotic cardiovascular disease (ASCVD) who have higher levels of the systemic inflammatory marker C-reactive protein (CRP) are at increased risk of adverse kidney outcomes, according to a report in the *American Journal of Kidney Diseases*.

The Swedish observational study included 83,928 adults with ASCVD who underwent routine testing of CRP between 2007 and 2021. The patients' mean age was 71 years; 54% were men. Patients were followed for at least 3 months after the initial CRP measurement.

Geometric mean serum CRP levels were analyzed for association with acute kidney injury (AKI) and with a composite outcome of a sustained increase of at least 30% in the estimated glomerular filtration rate (eGFR) or kidney failure.

Among the patients, 59% had a CRP level of 2 mg/L or higher, indicating systemic inflammation. Outcome analysis excluded CRP values potentially related to acute inflammation. Over a median follow-up of 6.4 years, there were 8731 kidney events, 10,757 AKI events, and 24,954 deaths.

Patients with higher CRP were at higher risk of both outcomes of interest. Compared with the reference value of 1 mg/L or less, adjusted hazard ratios for the composite kidney outcome were 1.16 at CRP values >1–3 mg/L, 1.24 for CRP >3–10 mg/L, and 1.35 for CRP >10–20 mg/L. Adjusted hazard ratios for AKI were 1.18, 1.34, and 1.37, respectively. Associations remained significant in sensitivity analyses and across a range of eGFR categories, except for advanced chronic kidney disease (CKD; eGFR of 15–29 mL/min/1.73 m^2).

Systemic inflammation plays a role in the development and progression of both ASCVD and CKD. CRP is an independent predictor of cardiovascular risk, in the presence or absence of CKD. However, there are conflicting data on CRP's associations with kidney outcomes.

The new study adds "real world" data highlighting higher CRP values associated with increased risk of adverse kidney outcomes in patients with ASCVD. The investigators conclude: "These results may inform clinical risk stratification along with monitoring and management to help protect kidney function in patients with ASCVD" [Mazhar F, et al. Systemic inflammation and the risks of adverse kidney outcomes in adults with atherosclerotic cardiovascular disease. *Am J Kidney Dis* 2025; 86:314–323.e1. doi: 10.1053/j.ajkd.2025.04.011]. ■

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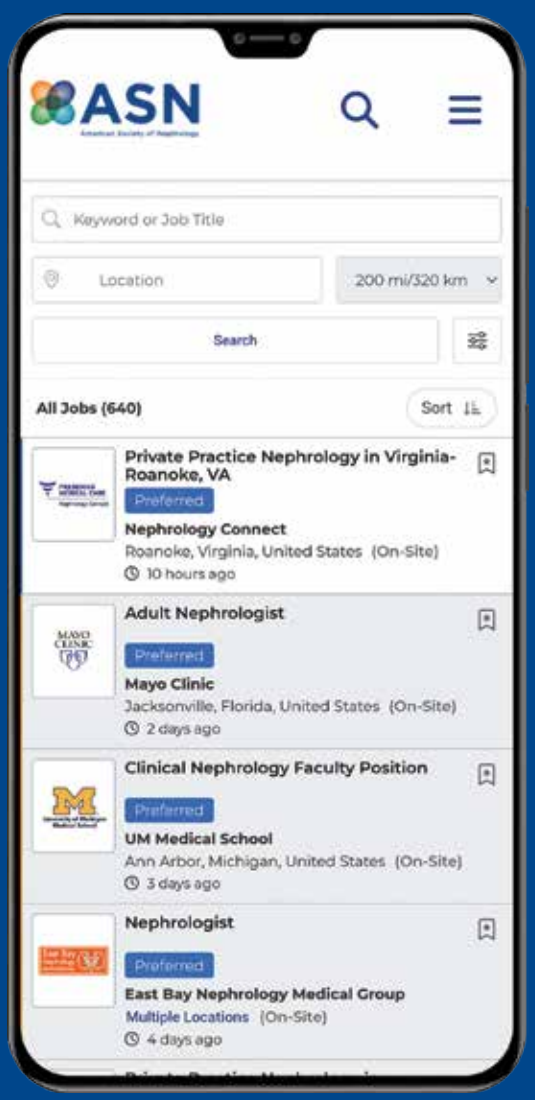

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APRIL, a proliferation-inducing ligand; BAFF, B cell activating factor; Gd-IgA1, galactose-deficient immunoglobulin A1; IgA, immunoglobulin A.

Reference: Cheung CK, et al. *Front Nephrol.* 2024;3:1346769. doi:10.3389/fneph.2023.1346769

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