ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

KIDNEY WEEK EDITION

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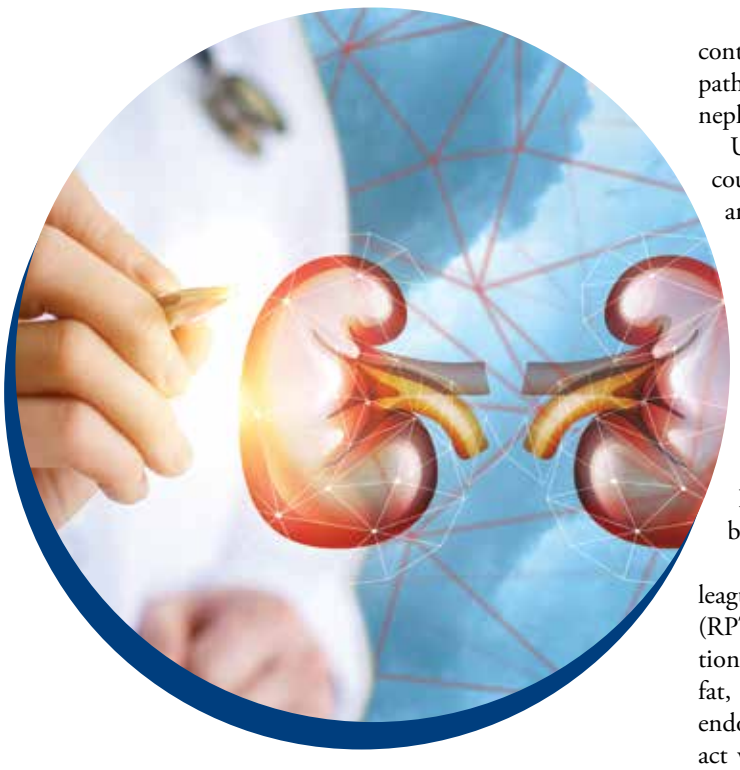
New Research Provides Clues to How Obesity Jeopardizes Kidney Health

By Tracy Hampton



Mounting evidence indicates that obesity has detrimental effects on the kidneys, and recent research is revealing the potential mechanisms involved. A new study published in the *Journal of the American Society of Nephrology* points to the important contribution of the endocannabinoid system to the pathogenesis of obesity-induced renal lipotoxicity and nephropathy.

Up to one-third of kidney disease in the United States could be related to obesity, likely due to hemodynamic and morphologic changes in the kidney.

"Obesity-associated renal structural and functional changes develop early in the course of obesity and the metabolic syndrome, and although multiple metabolic factors—such as insulin, glucose, and leptin—have been proposed to contribute to obesity-associated nephropathy, the underlying pathogenic signaling mechanisms have not been completely elucidated," said Joseph Tam, DMD, PhD, of the Institute for Drug Research at The Hebrew University of Jerusalem, in Israel.

In search of potential insights, Dr. Tam and his colleagues closely examined renal proximal tubular cells (RPTCs), which are responsible for active renal reabsorption and are especially sensitive to the accumulation of fat, an effect called lipotoxicity. Their work focused on endocannabinoids, endogenous lipid ligands that interact with the cannabinoid-1 receptor (CB1R), which is abundantly expressed in the brain and periphery, including the kidney.

When the team fed mice a high-fat diet, animals that lacked expression of the CB1R in RPTCs experienced significantly less obesity-induced lipid accumulation in the kidney as well as less kidney injury. "Using a novel mouse strain that lacks the CB1R from the RPTCs, we were able to demonstrate its pivotal role in the development of renal inflammation, fibrosis, and dysfunction during obesity," said Dr. Tam.

Additional experiments revealed the molecular signaling pathway involved in mediating the CB1R-induced kidney injury and lipotoxicity in RPTCs. Specifically, these deleterious effects associated with decreased activation of liver kinase B1 and the energy sensor AMP-activated protein kinase (AMPK), as well as reduced fatty acid β-oxidation.

"Ultimately, this was a very interesting paper that is building on our understanding of a new metabolic pathway in kidney injury," said Adam Whaley-Connell, DO, who was not part of the study and is a nephrologist and associate professor at the University of Missouri School of Medicine. "There are a number of studies that suggest the endocannabinoid system regulates proximal tubule function from mouse models to humans in diabetes; however, this current paper highlights the pathway may be regulated to a great extent by fat feeding and is an important regulator of lipid accumulation, fatty acid oxidation, and the AMPK mechanism that contributes to fibrosis in the kidney. In the search for new therapeutic targets this paper provides an intriguing new mechanism in obesity and/or diabetic kidney disease."

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Early Programs

ASN offers 10 Early Programs on Tuesday, October 31, and Wednesday, November 1, preceding the Annual Meeting (November 2–5). New Early Programs address several important areas of study:

- **Precision Medicine in Renal Diseases (Advances in Research Conference)** Critical advances in molecular and clinical medicine illuminate comprehensive genetic, molecular, structural, and clinical aspects of diseases. Learn about the latest strategies to integrate these multi-scalar data sets to define mechanisms that cut across knowledge domains and propel innovative approaches in novel clinical trials.
- **Advancing Clinical Research in Nephrology: Approaches and Methods**
  Epidemiology, clinical trials, and qualitative research define modern clinical investigation. Learn about innovative approaches to data acquisition, stakeholder engagement, systems biology, precision medicine, implementation science, the role of patient-reported outcomes and qualitative research, as well as fundamental concepts of clinical research.
- **The Dialysis Infection Crisis in the United States: A Call to Action**
  Nephrologists play a critical role as team leaders in transformational change required to address the urgent need to improve infection control in US dialysis facilities. This interactive program focuses on improving the safety of life-sustaining dialysis, protecting patients and health care personnel. Tools and education efforts will enable nephrologists to lead the pursuit of zero preventable infections.
- **What You Need to Know about Diabetes and Diabetic Kidney Disease**
  This program addresses the background epidemic of diabetes mellitus, the pathophysiology of diabetic CKD, current approaches to diabetic CKD and hypertension, new drugs in development, the growing use of hypoglycemic agents in diabetic CKD, and unique dialysis and transplant problems facing patients with ESRD due to diabetes.

ASN Communities Lounge

Thursday, November 2, to Saturday, November 4, 9:30 a.m.–2:30 p.m.

The new ASN Communities Lounge extends the exciting professional network that is expanding daily through online ASN Communities. Visit and connect with those working in your area of study, or working in areas you want to know more about. The lounge is located in the exhibit hall and features:

- ASN Community Leaders
- Central Connectivity Bar
- Meeting Quads
- Relaxation Zone

Stop by booth 917 to explore the ASN Communities world and enhance your Kidney Week experience.

In addition to the new items above, don't forget to check out these events:

- Welcome Reception in the exhibit hall on Thursday, 6:30–7:30 p.m.
- Daily state-of-the-art lectures during the plenary sessions (Thursday–Sunday, 8:00–9:30 a.m.)
- Daily poster presentations with more than 3000 posters (Thursday–Saturday, 9:30 a.m.–2:30 p.m.)

Obesity

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According to Dr. Tam, the work provides a novel approach to slow the development of renal injury through chronic blockade of peripheral CB1Rs. "And, it also supports strategies aimed at reducing the activity of the endocannabinoid system, specifically in the kidney, to attenuate the development of RPTC dysfunction in obesity."

Allon Friedman, MD, who was not involved with the work and is a nephrologist and clinical investigator at Indiana University School of Medicine, noted that the intimate connection between rising rates of obesity and chronic kidney disease makes it likely that this topic will become increasingly prominent in the coming years.

"These intriguing animal studies expand our understanding of how endocannabinoid physiology influences kidney health," he said. "The next step will be to extend these findings in humans through the testing of endocannabinoid receptor antagonists." In his 2011 *Kidney News* article, Dr. Friedman pointed to other possible factors, including alterations in levels of adipocyte-related cytokines such as leptin and adiponectin (as well as other hormones) and upregulation of the renin-angiotensin axis and sympathetic nervous system activity. Many unanswered questions remain surrounding both the causes of obesity-related kidney disease and its optimal treatment.

Visceral Fat Is Linked to Inflammation in Dialysis Patients, While Subcutaneous Fat Marks Nutritional Status

In dialysis patients, visceral fat is a marker of inflammation while subcutaneous fat is a marker of nutritional status, suggests a study in *American Journal of Kidney Diseases*.

The cross-sectional study included 609 adult hemodialysis patients enrolled in the US Renal Data System's ACTIVE/ADIPOSE study. Participants underwent several measurements: body mass index (BMI), waist circumference as an indicator of visceral fat, and percentage body fat as an indicator of subcutaneous fat. The two fat measures were evaluated for association with markers of inflammation, nutrition, and adiposity-related hormones.

Body mass index was directly related to the inflammatory markers C-reactive protein and interleukin-6 (IL-6), but not with markers of nutrition, i.e., prealbumin or albumin. BMI was inversely associated with adiponectin and directly related to leptin. In a model including proxies for both visceral and subcutaneous fat, percentage body fat—the indicator for subcutaneous fat—was unrelated to C-reactive protein, but was inversely associated with IL-6.

Also in this model, waist circumference was associated with markers of inflammation but was inversely associated with prealbumin and albumin. Percentage body fat was directly related to these nutritional markers. Waist circumference was indirectly related to adiponectin and indirectly related to leptin.

Dialysis patients with BMI higher than the normal range generally have a higher survival rate, a phenomenon called the "obesity paradox," which has confounded researchers and practitioners. Yet BMI is a general marker of adiposity, and does not distinguish between subcutaneous and visceral fat, which may have differing metabolic and inflammatory characteristics. Determining the type of fat—visceral or subcutaneous—may help unravel the obesity paradox, but longitudinal studies are needed to clarify the associations between measures of body fat and markers of inflammation.

Added to previous findings, the results of this cohort study of dialysis patients suggest that "higher subcutaneous fat may account for the observed survival advantage associated with higher BMI."

Delgado C, et al. Associations of body mass index and body fat with markers of inflammation and nutrition among patients receiving hemodialysis. *Am J Kidney Dis* 2017; DOI: http://dx.doi.org/10.1053/j.ajkd.2017.06.028].

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State of Kidney Care 2017
Kidney Care Provider CMOs

By Allen R. Nissenson, MD; Franklin Maddux, MD; Doug Johnson, MD; and Brigitte Schiller, MD, on behalf of the US Kidney Care Provider CMOs

Last year the Kidney Care Provider Chief Medical Officers (CMOs) offered a perspective on the State of Kidney Care in 2016. Some issues have remained the same in 2017, but the fast pace of change in many areas warranted an update. Health care in the US is undergoing transformation as Medicare moves from volume-based fee-for-service to value-based payment systems. In the next two years, it is possible that more than 50% of Medicare payments could be made in Advanced Alternative Payment Models (APMs) regardless of what happens as a result of efforts to repeal and replace the Affordable Care Act. There currently are 561 Accountable Care Organizations (ACOs) (120 of these are risk bearing) with a total of 12.3 million patients receiving care in an ACO. In 2017, 85 new ACOs were started.

For kidney care, 24 new ESRD Seamless Care Organizations (ESCOs) started in 2017, bringing the total to 37. Currently, 46,000 patients receive care in an ESCO and 1291 physicians are owners in ESCOs. All but three of these ESCOs are Advanced APMs, allowing for the possibility of nephrologist owners to receive a 5% bonus payment from Medicare in 2019. Should the Center for Medicare and Medicaid Innovation (CMMI) choose to extend and expand the ESCO program after 2018, as many as 15% of all Medicare ESRD patients could be enrolled in an ESCO over the next 5 years.

In addition, we see increasing appearance of Medicare Advantage Special Needs Plans (cSNPs) for ESRD patients and the attempt to create additional opportunities to deliver value-based care through the PATIENTS ACT, an alternative value-based care model to ESCOs and cSNPs.

This rapid pace of innovation in kidney care creates an incredible opportunity for the discipline of nephrology and the nephrologist to help shape care delivery and payment for kidney patients as well as other complex chronically ill populations, creating significant improvements in patient outcomes, while responsibly stewarding resources. There are a number of challenges and opportunities in the coming year from the perspective of the dialysis provider CMOs.

Challenges

1. **Transformation of the health care system and the practice of nephrology:** The systemwide transformation of US and global health care means providers are increasingly accountable for clinical outcomes as well as the total costs of care. Nephrologists need to be leaders in this transformation, which will impact them in all of the realms in which they practice: dialysis facilities, offices, and hospitals. While individual nephrologists and practices will be differentially affected by this transformation, all will be affected to some extent and need to be prepared to thrive in the new world of care delivery and reimbursement/payment systems.

2. **Where nephrologists and kidney care providers fit in the new health care system:** Nephrologists and kidney care providers will be at the forefront of the new health care system because of the disproportionate cost of advanced CKD and ESRD patients. Innovative solutions for improving care and controlling costs are needed. Going forward, nephrologists and dialysis providers will need to work together to ensure that these solutions are identified, tested, and implemented. Nephrologists will have more options regarding their clinical work environment, with an increasing number likely to find salaried positions with health systems, integrated health care organizations, physician groups, hospitals, or dialysis providers. Career advancement programs need to be broadened to inform nephrologists of the benefits and pitfalls of these options.

3. **The critical role of health information technology:** Integral to the success of integrated care is the ability to seamlessly share patient information through electronic health records (EHRs). Nephrologists often use multiple EHRs in the different settings in which they practice and are perhaps more aware of the need for seamless integration of these information systems than other physicians. Nephrologists need to lead the design of more usable systems and algorithms to enhance sharing of information in real-time fashion, an effort that should include interoperability, a common lexicon, and agreed-upon metrics and business rules so meaningful use of the massive amount of available data is possible.

4. **Influence of regulatory oversight and public data on patient care:** There is a need for increasing rigor in the development and selection of quality metrics to ensure they have an impact on the quality of patient care. Oversight of quality in the payment system through the Quality Improvement Program has been one of the primary approaches by the Centers for Medicare & Medicaid Services (CMS), but further refinement of QIP measures and methods used to calculate them needs to be informed by evidence, sound methodology, and in the future include patient-reported outcomes. By engaging in the research and development of such accountability systems, nephrologists can lead the development of important quality measures rather than waiting for CMS to dictate them. Nephrologists may act as individuals and through professional organizations such as ASN and the Renal Physicians Association (RPA), as well as through national coalitions such as Kidney Care Partners, Kidney Care Coalition, and the National Renal Administrators Association (NRAA). Nephrologists must be active advocates for patients and for the discipline of nephrology. Accountability should be an area developed and structured through the discipline, not by regulators.

5. **The nephrology workforce:** Care of patients with kidney diseases and kidney failure will be dependent on teams including nurses (RNs and NPs), social workers, care coordinators, patient care navigators, health coaches, patient care technicians, clinical specialists (e.g., podiatrists, cardiologists, endocrinologists, vascular surgeons), insurance/benefits experts, and others who focus on social determinants of health, such as housing, nutrition, transportation, and employment. Another aspect of integrated team-based care is improved palliative care for symptom management during life and care at the end of life. The nephrologist needs to be the leader and coordinator of this team.

   The lack of interest in nephrology careers among medical students and residents will make it difficult to reach sufficient numbers and quality of nephrologists to meet needs spanning clinical care and administrative functions. Attracting more trainees to nephrology requires changing the approach to teaching the discipline. Too often the emphasis on basic physiology does not "connect the dots" with the implications of organ dysfunction leading to the many manifestations of CKD and ESRD that patients exhibit and that make the specialty so fascinating, yet complex. Students and residents must be exposed to outpatient CKD management and to care of dialysis and transplant patients outside the inpatient setting. In this way the successful and rewarding outcomes of kidney patient care are better conveyed. Articulating the leading role of nephrology in defining and implementing value-based care, palliative care, and driving public policy should also attract talented trainees who are looking for new career paths.

6 **Integrated care and the ideal role of the nephrologist:** The nephrologist's role varies depending on the site of focus of care. A nephrologist acting as a dialysis facility medical director serves as the population health leader and plays an additional role as the principal care provider for each patient for whom they are responsible. This role is distinct from primary care, and training programs need to educate nephrologists about these distinctions. Outside the dialysis facility the nephrologist is now likely to be even more involved in care coordination, particularly with the advent of MACRA, which created incentives to participate in such programs, including Advanced APMs. An Alternative Payment Model (APM) is a payment approach that gives added incentive payments to provide high-quality and cost-efficient care. APMs can apply to a specific clinical condition, a care episode, or a population. Advanced APMs are a subset of APMs, and let practices earn more for taking on some risk related to their patients' outcomes. Nephrologists earn a 5% incentive payment by going further in improving patient care and taking on risk through an Advanced APM.

There is a need for greater opportunities for nephrologists to access APM models of care such as the ESCO program, where essentially all involved providers have been classified as qualifying providers for their participation in the program, providing an opportunity for nephrologists to align financial incentives with clinical imperatives. Nephrologists must understand the impact of non-traditional adjacent diseases, other medical conditions, or social circumstances on health outcomes of kidney patients. To do so, nephrologists must be more involved in the overall assessment and care of patients, performing as the principal care physician. Training of nephrologists must change to prepare them for this new role. As physician training has transitioned to greater emphasis on outpatient care, so must nephrology training. This shift requires a partnership among kidney care providers, nephrology fellowship training programs, and ASN to facilitate a larger clinical and administrative role for trainees in dialysis units.

7 **Innovation in the kidney space:** Bundling of payments for dialysis—and the resulting uncertainty about reimbursement potential for new products—has had a chilling effect on pharmaceutical and medical device companies' interest in pursuing new therapies for kidney patients. But the advent of integrated care systems for kidney patients has fostered a more recent renewal of interest in innovation. In integrated care settings, any innovation that creates value generates interest: A more expensive dialyzer is a valuable investment if the result is a healthier patient who lives longer and does not require hospitalization. Removing regulatory barriers to innovation is an important driver of innovation for the future.

Opportunities

1 **Improving care for patients with CKD:** Few patients with advanced CKD (GFR <45) know they have kidney disease, yet there is no systematic approach to population health for the identification, prevention, early diagnosis, and better management of patients with CKD. No reimbursement mechanism exists to incentivize or support such a comprehensive program. Nephrologists know that working upstream in the continuum of CKD is essential for improving clinical outcomes and controlling total costs of care. A joint effort is needed on the part of nephrologists and the kidney community (particularly ASN, the Renal Physicians Association, and the National Kidney Foundation) to develop a CKD prevention, early detection, and management program, including advocating for reimbursement (including shared savings) by CMS and commercial insurers. Integration of care among various providers will lead to more opportunities for nephrologists to have an impact on this population and slow the progression of CKD.

2 **Improving care for patients with acute kidney injury:** Kidney health providers are now treating a larger number of patients with AKI in outpatient facilities. It is essential that we recognize that a patient with AKI has different needs than a patient with ESRD. In a collaborative partnership, nephrologists and providers need to work on a better model of care for patients with AKI, with the primary goal of recovering kidney function where possible or preparing for chronic renal replacement therapy (RRT) when necessary. Sharing of best practices will inform the development of an improved model of care for AKI patients. ASN can play a critical role in sharing what we are learning to a broader audience.

3 **Improving access to home dialysis:** Most nephrologists and clinicians would choose home dialysis for themselves, yet few patients on dialysis are able to benefit from dialysis at home. A patient dialyzing at home has more autonomy, is more likely to continue to work, and has more satisfaction in their kidney care. Nephrologists and other providers should work together to identify opportunities to make it more likely that patients can dialyze at home. They should rethink curriculum structure and requirements for training and competence in home dialysis because many training programs do not have a sufficiently large home dialysis program to adequately train fellows. In addition, as recent events have illustrated, availability of adequate supplies to carry out home dialysis and lack of innovation in delivery systems has hampered the further growth of these modalities.

4 **Increasing access to kidney transplant:** Most agree that transplant is the optimal therapy for patients with kidney failure who are medically suitable. Yet few patients benefit from transplants. Only 2.6% of patients with kidney failure receive a preemptive transplant as treatment; the remaining 97.4% start dialysis. We need to emphasize transplantation as a care modality for patients with ESRD and ensure nephrologists view it this way.

Nephrologists, organ procurement organizations, transplant programs, and kidney health providers should work together to develop new approaches to improve access to kidney transplantation through both living and deceased kidney donation. Several areas could be significantly improved by such a collaborative approach including evaluation expectations, waitlist management, better utilization of kidneys with high KDPI scores, health information exchange around transplant, desensitization, and preparing the recipient with a failing transplant for return to RRT. An incentive system for nephrologists could be developed and implemented to encourage transplantation, and research efforts such as (Re)Building a Kidney (an NIDDK-supported consortium) to expand the capacity for biological kidney replacement must be supported. Approximately 100,000 patients are on the transplant waitlist, yet only 17,000 kidney transplants are performed annually, resulting in an unacceptably long wait and unnecessary morbidity and mortality.

5 **Improving end-of-life care:** Patients over 80 with multiple comorbidities have comparable outcomes if they receive comprehensive conservative care instead of dialysis, yet few choose this option, partly owing to the dearth of nephrologist training in non-dialytic and palliative care. Patients on dialysis at the end of life utilize hospice much less frequently than other patients with similar comorbidities and cost of care. Nephrologists and other providers should work together to improve end-of-life, both for patients with CKD and for patients on dialysis. ASN could explore curricula elements that inform nephrology trainees about medical strategies that extend the duration and quality of life without dialysis.

6 **Informed choice for patients with kidney disease:** Kidney patients need to be assured they have full access to options regarding their care including transplantation, home or in-center dialysis, and conservative therapy. This need also extends to patients' ability to choose integrated care plans, Medicare Advantage plans, or maintainence of private insurance (including the use of charitable premium assistance where appropriate) when it is in their best interest.

7 **Promoting innovation in CKD and ESRD care:** A concerted focus on continuous innovation in the care of patients with kidney disease is needed. There should be strong support for the existing vehicles for developing innovative approaches to improving outcomes, but also efforts to advance basic science understanding of CKD and ESRD and pragmatic solutions to care delivery and financing problems. Examples of existing programs are the Kidney Health Initiative, CMMI special projects, Nephrologists Transforming Dialysis Patient Safety, and the Center of Dialysis Innovation. More such programs are needed.

Additional specific areas of focus given a high priority by the CMOs include the following:

a. Revisiting the definition of "adequate" dialysis.
b. Defining evidence-based criteria for alternative dialysis regimens.
c. Optimizing the use of self-care modalities.
d. Defining, utilizing, and harmonizing meaningful quality metrics that reflect care that is relevant and important to patients.

Achieving the goals stated here will require a close working relationship among kidney health providers, nephrologists, and nephrology fellowship training programs. By establishing a closer partnership, kidney care provider CMOs and ASN can build toward a stronger future for providers, nephrologists, and patients. An important aspect of this link is the establishment of a committee of representatives of both groups with the aim of enhancing career development for early career nephrologists and nephrology trainees. Such a program should aim to enhance skills in the clinical management of patients with advanced CKD, foster a better understanding of the financial and legal impacts of the changing health care system, and improve opportunities for research in quality metrics and improvement.

We are currently at a time of rapidly accelerating change in American health care, and the care of kidney patients is at the forefront of this ongoing transformation. The movement to value-based care offers challenges to our discipline but the clear opportunity to significantly improve the care and lives of patients with kidney diseases. The CMOs are interested in strengthening our collaboration with ASN. Possible opportunities to increase collaboration include:

a. Regular meetings of ASN leadership and kidney care provider CMOs.
b. Definition of a common set of issues to be addressed jointly.
c. Exploration of how the kidney care organizations can assist ASN in reaching out to potential nephrology trainees.
d. Exploration of how the kidney care organizations can assist ASN in ensuring that trainees have access to the necessary training in CKD and ESRD patient care that will likely be the focus of practice for many.
e. Serving on the ASN Career Advancement Committee.
f. Contributing to the planning process for ASN Kidney Week.
g. Partnering to work with CDC, including the efforts of the Healthcare Infection Control Practices Advisory Committee.

State of Kidney Care 2017
American Society of Nephrology

By Barbara Murphy, MD, FASN, with David White

The more things stay the same, the more things change—or, at least, the more things need to change. That may be turning an old adage on its head, but turning things upside down seems to capture events since the last report on the state of kidney care in 2016.

For things to stay the same is not an acceptable state in nephrology, considering there are an estimated 40 million Americans living with kidney diseases and for nearly 700,000 of those individuals access to dialysis or a kidney transplant is their only chance to live. With a life expectancy of 5 to 10 years on dialysis, our patients with kidney failure must constantly confront the national organ shortage crisis: every 14 minutes a patient is added to the kidney wait list and every day, 13 patients die waiting for a kidney transplant.

These numbers are unacceptable, and we must be willing to say so.

As a chair of medicine at Mt. Sinai, member of the American Society of Nephrology (ASN) Council, and a transplant nephrologist/immunologist, I can say clearly and unequivocally, we need to "get real" when talking about kidney diseases; the devastating toll on patients, their families, and caregivers in the United States and across the globe; and the challenges we face confronting this epidemic.

Where there is change, some is good and some is less so. ASN supports the move away from a volume-based to a quality-based payment system in the new Quality Payment Program (QPP). The growth of alternative payment models (APMs) and the testing of physician-focused payment models under the QPP may well provide innovative approaches to care and less strenuous reporting requirements for clinicians.

However, the QPP is still a new, evolving program that has a way to go to address the needs of nephrologists reporting in the Merit-based Incentive Payment System (MIPS) as there are few nephrology-specific quality measures in the quality category and literally no nephrology-specific measures in the cost category—two of the four reporting categories that determine whether clinicians will see a bonus or a pay cut.

In the last year, Congress has considered significant changes to health care in the name of "repeal and replace" of the Affordable Care Act, generally without much debate or input from stakeholder groups. This changing environment has left health care professionals, insurers, and patients concerned and weary. ASN has worked with peer societies to preserve important policies, with varying results: access to Medicaid remains in place and patients cannot be denied insurance coverage for "pre-existing conditions" like kidney disease or having donated a kidney—but improvements to the existing law are clearly needed.

Moreover, the big picture changes needed in nephrology are going to require us to be the agents of change. It is time for us to decide whether we are up to the challenge so eloquently expressed by James Baldwin: "Not everything that is faced can be changed, but nothing can be changed until it is faced."

As the chief medical officers (CMOs) observe, the challenges ahead are multitudinous—touching on a transforming health care system and the role of the nephrologists in that system, the role of both government regulators and health information technology, and the need for innovation in kidney care therapies and kidney care delivery models. ASN and the CMOs also see similar opportunities in this evolving environment. A great deal of opportunity exists to improve care for patients across the kidney care spectrum: kidney diseases, acute kidney injury (AKI), kidney failure, transplantation, and end-of-life care.

And while we need innovation in both therapies and care delivery, too often it is easier to use the lack of innovation in kidney care as an excuse. We need to get patients into our care earlier, identify reversible conditions early, and more aggressively manage their conditions, while simultaneously working to identify new therapies.

ASN is also wrestling with how best to articulate the role of nephrology and the nephrologists during this transformative period. Since kidney patients often present multiple comorbidities and their care cross-cuts multiple medical disciplines, it is sometimes challenging to clearly articulate what a commonly agreed upon role for nephrology and its clinicians should be. In an era of evolving care models, ASN agrees with the CMOs that it is very important that nephrologists find their voice and express their role and value. This demonstration is critical to demonstrating the value of including nephrologists in care models.

Innovation must occur if we are to impact the current epidemic, that much is very clear. We cannot rationalize the value of nephrology as an essential part of the care plan for kidney diseases if the status quo is maintained. The lack of new therapeutic approaches will lead to the stagnation of the specialty and continued decline in interest from fellow candidates.

Recognizing the relative lack of innovation and new therapies in nephrology compared to other medical subspecialties, ASN launched the ASN Innovation and Discovery Task Force this summer. This task force is instrumental to achieving the second goal of the ASN Strategic Plan: "Transform kidney research through discovery and innovation to prevent, treat, and cure kidney diseases."

The task force has reviewed ASN's portfolio of current activities as well as external initiatives such as accelerator concepts that offer financial and other incentives to identify, select, and accelerate a portfolio of solutions. The task force also has examined venture philanthropy, which takes concepts and techniques from venture capital finance and business management and applies them to early stage funding for biotechnology and pharmaceutical companies to develop breakthrough drugs. These and other programs conducted by peer medical societies, patient organizations, foundations, and other innovators are among those the task force is reviewing.

With innovations in kidney therapies, there also comes a need for innovation in care delivery—including preemptive transplantation, increased access to home dialysis and telemedicine, and comprehensive care models. In care delivery, as clinicians, we know how dangerous transitions can be, whether from the hospital to the dialysis unit, or onto dialysis in the first place, or from dialysis to treat AKI onto maintenance dialysis for kidney failure, to name just a few.

The ASN leadership and I believe that a comprehensive kidney care delivery model could be much broader than an ESRD Seamless Care Organization (ESCO)—encompassing patients with advanced kidney diseases and including kidney transplant recipients, coordinating their transitions as their conditions progress, and managing and slowing progression of kidney diseases and other complex chronic conditions that are common in the kidney patient population.

Reflecting the fact that transplantation is, for many patients, the optimal therapy for kidney failure, such a care delivery model would include transplant recipients for the duration of their lives, providing continuity of care and aligning incentives. A comprehensive kidney care delivery model would present a unique opportunity to provide better, more cost-effective, and more patient-centered care than is possible under the current delivery system.

ASN and nephrologists must better quantify their value and health care system savings. In a value-based system, not being able to quantify your value is a losing proposition. With Medicare spending $103 billion annually on kidney patient care (including $32.8 billion on care for beneficiaries with ESRD), those striking statistics might appear to be sufficient quantification, but looking at society's complacency with the current environment suggests it is not.

Instead, the kidney community and nephrologists must begin to demonstrate that coordinated, team-based care that actively involves the nephrologist in the management of patients with kidney disease is an opportunity for cost savings within health care systems. We know firsthand that these patients represent some of the highest utilizers of resources in at-risk care models, and it will take our involvement and commitment to address ways to reduce those demands while providing our patients with the best care possible.

There are multiple areas of potential collaboration for CMOs and ASN from working on creative care models to advancing opportunities for innovation, all with the nephrologist voice and what's best for patients front and center. ASN welcomes the opportunity to work with CMOs and other kidney community members. There is much work to be done and more hands, hearts, and heads are welcome.

Barbara Murphy, MD, FASN, is a member of ASN Council and Council liaison to the ASN Policy and Advocacy Committee. She is affiliated with the Icahn School of Medicine at Mount Sinai in New York City. David White is a Policy and Communications Specialist at ASN.

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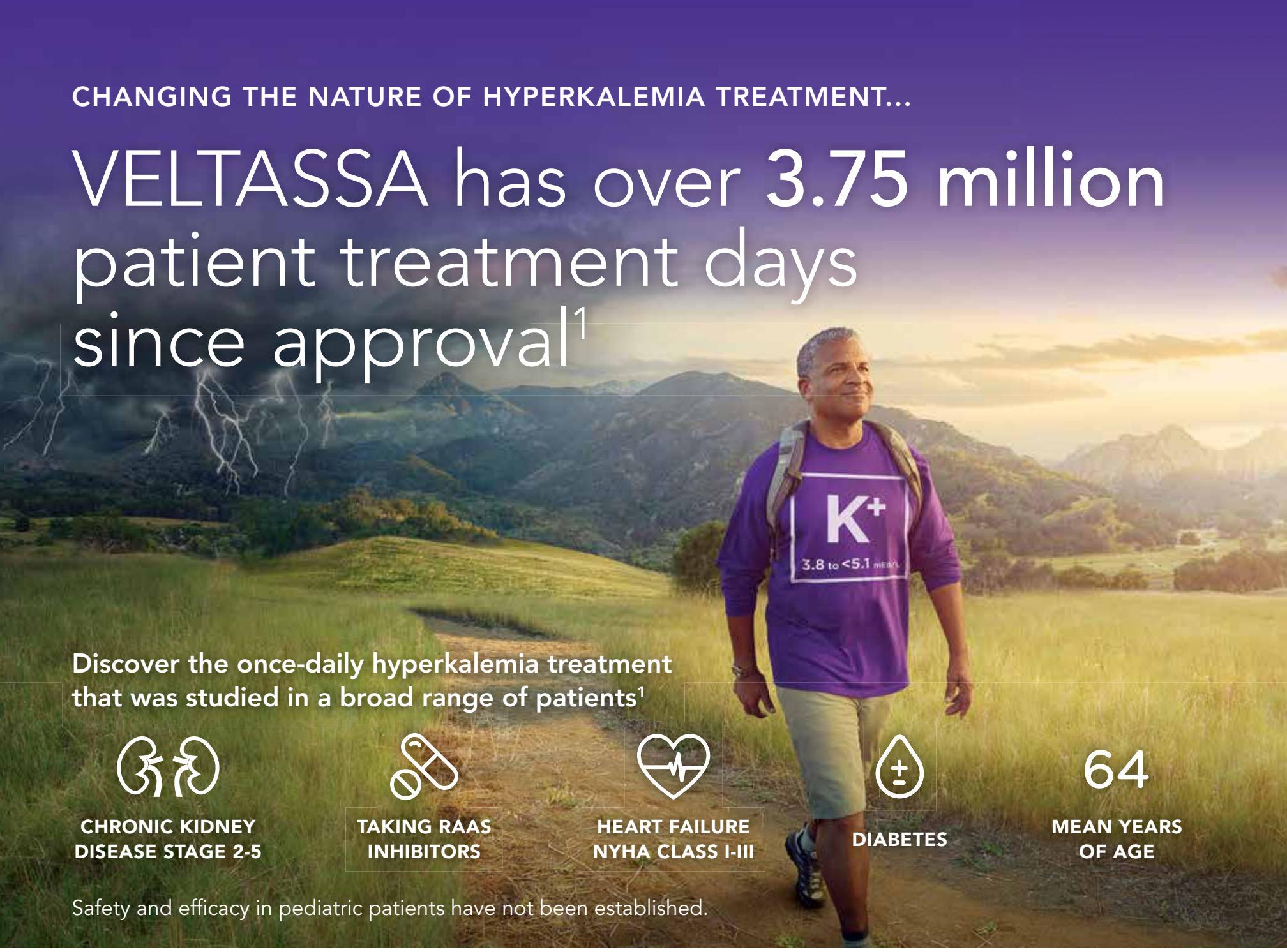

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VELTASSA is indicated for the treatment of hyperkalemia.

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Reference: 1. Data on file as of April 2017, Relypsa, Inc.

Findings

Anti-IL1β Therapy Lowers Cardiovascular Risk after MI

Anti-inflammatory therapy with canakinumab—targeting the interleukin-1β (IL-1β) innate immunity pathway—reduces cardiovascular events in patients with previous myocardial infarction (MI), reports a trial in *The New England Journal of Medicine*.

The industry-sponsored "Canakinumab Antiinflammatory Thrombosis Outcome Study" (CANTOS) enrolled 10,061 adults with a history of MI. All had a persistent proinflammatory response, with high-sensitivity C-reactive protein of 2 mg/L or higher. Patients were randomly assigned to receive canakinumab every 3 months, 50, 150, or 300 mg sc; or placebo. Rates of nonfatal MI or stroke or cardiovascular death were compared between groups.

All three canakinumab doses reduced high-sensitivity C-reactive protein, with no effect on lipid levels. Primary outcome incidence rates at 3.7 years of follow-up were 4.50 events per 100 person-years in the placebo group, 4.11 events with canakinumab 50 mg, 3.86 events with the 150 mg dose, and 3.90 events with the 300 mg dose. Hazard ratios compared to placebo were 0.80 (not significant), 0.85, and 0.86, respectively.

A prespecified analysis combined the primary outcome with a secondary endpoint of hospitalization for unstable angina leading to urgent revascularization. For the composite outcome, only canakinumab 150 mg was superior to placebo: hazard ratio 0.83. All-cause mortality was not significantly different for canakinumab versus placebo. Rates of neutropenia and death from infections or sepsis were higher with canakinumab.

This clinical trial supports the hypothesis that treatment to reduce inflammation but not lipid levels can reduce cardiovascular events in patients with previous MI. Other approaches to anti-inflammatory therapy might also be effective in lowering cardiovascular risks. Anti-IL1β therapy with canakinumab is associated with an increased risk of serious infections and sepsis [Ridker PM, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med* 2017; DOI: 10.1056/NEJMoa1707914].

Chronic HCV Linked to Higher CKD Risk

Chronic hepatitis C virus (HCV) infection is associated with an increased risk of chronic kidney disease (CKD), with the extent of risk depending on viral load and genotype, reports a study in *Kidney International*.

The researchers analyzed data on 13,805 Taiwanese adults from a prospective, community-based cohort study. Mean age at enrollment was 47.5 years. Based on detectable HCV load, 431 patients had chronic HCV infection. Chronic HCV infection, viral load, and phenotype were evaluated for association with CKD, defined as consecutive proteinuria or an estimated glomerular filtration rate of less than 60 mL/min/1.73 m^2.

Subjects with chronic HCV infection had about a twofold increase in CKD: adjusted prevalence odds ratio (POR) 1.91. Risk was highest for chronically infected patients in the highest tertile of serum HCV RNA: POR 3.44.

Among participants with high HCV viral load, PORs were 2.62 for those with HCV genotype 1 and 4.99 for those with genotype 2. On subanalysis including only those with detectable serum HCV RNA, the risk of CKD was about three times higher for those with genotype 2 versus genotype 1.

There is debate over the association between HCV and CKD. Taiwan is an area endemic for HCV and has the highest prevalence of kidney failure worldwide.

This cross-sectional study suggests that chronic HCV infection is an independent risk factor for CKD in Taiwan. Kidney disease risk is particularly high for patients with high HCV viral load and/or HCV genotype 2. The authors call for a prospective study to clarify whether HCV viral load and genotype are associated with an increased likelihood of developing CKD and kidney failure [Lai T-S, et al. High hepatitis C viral load and genotype 2 are strong predictors of chronic kidney disease. *Kidney Int* 2017; 92:703–709].

Tradeoffs in Medication Adherence after Acute Myocardial Infarction Confer Different Mortality Risks

For patients with acute myocardial infarction, nonadherence to beta blockers doesn't reduce mortality—as long as they are taking their prescribed angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) and statins, reports a study in the *Journal of the American College of Cardiology*.

The researchers analyzed "tradeoffs in adherence" to multiple preventive therapies using data on nearly 91,000 Medicare beneficiaries aged 65 or older with acute myocardial infarction between 2008 and 2010. All patients survived at least 180 days after being hospitalized for acute myocardial infarction and received prescriptions for ACEIs/ARBs, beta blockers, and statins.

Medicare Part D prescription claims were used to analyze adherence to the three classes of drugs, and adherence was defined as at least 80% of days covered for each medication. Mortality was compared for patients who were adherent to none, one, two, or all three medications. Follow-up for mortality continued for 18 months after the 180-day postdischarge period.

Overall, 51.5% of patients were nonadherent to at least one of the three medications: 30.7% were nonadherent to ACEIs/ARBS, 23.8% to beta blockers, and 23.0% to statins. During mean follow-up of about 1 year, 10.6% of patients died. Adjusted mortality was 9.3% for patients adherent to all three medications, compared to 14.3% for those nonadherent to all three therapies.

About 9% of patients were adherent to ACEIs/ARBs and statins, but not beta blockers. In this group of patients, mortality was not significantly different from that for those who were adherent to all three medications. Adjusted hazard ratios for mortality were 1.65 for those nonadherent to all three therapies, 1.32 for those adherent to beta blockers only, and 1.26 for those adherent to statins only. For those adherent to ACEIs/ARBS only, the adjusted hazard ratio was 1.19; 1.17 for those adherent to beta blockers and statins only, and 1.12 for those adherent to ACEIs/ARBs and beta blockers only.

The benefits of adherence to ACEIs/ARBs were greater in patients with diabetes on subgroup analysis. In contrast, the directions of the associations were generally similar in other subgroups. The effects of adherence tradeoffs tended to be larger in men than women and in older compared to younger patients.

Suboptimal adherence to secondary preventive therapies after acute myocardial infarction is well documented. Few clinical trial data are available to guide the balance of risks and benefits of these medications, particularly in older adults taking many different prescriptions.

The new findings confirm that only about half of older adults are adherent to all three recommended medications after acute myocardial infarction. Those who are adherent to ACEIs/ARBs and statins show no significant reduction in one-year mortality, compared to those adherent to all three medications. All other nonadherence groups show increased mortality risks.

"[L]ong-term adherence to ACEIs/ARBs and statins may be more important than adherence to beta blockers after acute myocardial infarction," the investigators conclude. They emphasize the need for further studies to clarify the clinical implications of their findings [Korhonen MJ, et al. Adherence tradeoff to multiple preventive therapies and all-cause mortality after acute myocardial infarction. *J Am Coll Cardiol* 2017; 70:1543–1554].

ASN in Review

Since last year's Kidney Week, ASN has continued to focus on the five goals in its strategic plan.

Goal 1—Lead the kidney community by focusing on education, communications, policy, and collaboration

Report Outlines Deficiencies in Kidney Research Funding

The U.S. Government Accountability Office (GAO) report "*National Institutes of Health: Kidney Disease Research Funding and Priority Setting*" lays out the inadequacies of federally funded research for kidney diseases in the face of a staggering burden on patients and taxpayers.

Working with a bipartisan group of legislators to request the GAO report, ASN is now using it to advocate for greater congressional funding for the National Institutes of Health, including dedicated "Special Kidney Program" research funds of $150 million per year for 10 years.

ACA Repeal, NIH Funding, and Executive Orders

To advocate for kidney patients and professionals, ASN kept a close watch on congressional efforts to repeal and replace the Affordable Care Act and informed ASN members of important milestones. ASN also independently and jointly with other organizations sought increases in National Institutes of Health (NIH) funding and opposed the Executive Order on Immigration that banned travel from six majority-Muslim countries.

ASN used its set of Guiding Principles on Healthcare Reform to evaluate all proposals advanced in Congress this year. In its request for a $2 billion increase in NIH funding, ASN included a proportional increase for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). ASN aimed to protect the free flow of science and information in support of an open global society in opposing the travel ban.

ASN, ERA-EDTA, and ISN Collaboration

June 1, 2017, marked the one-year anniversary of the Declaration of Collaboration signed by ASN, the European Renal Association–Renal Dialysis and Transplant Association (ERA-EDTA), and the International Society of Nephrology (ISN). The societies also created a Universal Lexicon for Terminology to facilitate collaboration and understanding.

To improve the standard of care for kidney patients worldwide, the societies are currently collaborating in three areas: using high-impact data to communicate the kidney disease pandemic, comparing realities across the global nephrology workforce, and prioritizing ethical issues confronting nephrologists around the world.

WIN-ASN Career Advancement Webinars Available Online

Women in Nephrology (WIN) and ASN launched free professional advancement webinars that offer advice on directing or adjusting career pathways and negotiating to advance career goals. The webinars offer real-world advice from successful nephrologists and an expert in negotiating for career development with the aim of helping individuals make a difference in the lives of people with kidney diseases.

Topics include Career Choices in Nephrology: Am I on the Right Path?, How to Get Promoted, and Negotiating for Leadership Success. Access the webinars at www.asn-online.org/education/distancelearning/webinars/.

Expanded Journal Offerings

JASN and *CJASN* introduced visual abstracts and Perspectives to enhance the journals' appeal to authors and readers. Josephine P. Briggs, MD, was named Editor-in-Chief of *JASN*, and under her leadership, the journal will begin publishing significance statements to explain the relevance of each paper's findings to a broad readership.

Besides increasing the number of podcasts, *CJASN*, under the leadership of Editor-in-Chief Rajnish Mehrotra, MD, FASN, will continue to publish high quality clinical kidney research in areas such as AKI and ICU nephrology, hypertension, and transplantation.

Twitter Chats on Kidney Controversies

The increasingly popular #AskASN Twitter chats hosted by ASN and the Nephrology Journal Club (NephJC) delved into controversies in kidney care: Anticoagulation in Dialysis, Atrial Fibrillation in ESRD, and Preeclampsia and sFlt-1. Other topics included chats with ASN President Eleanor Lederer, MD, FASN, *CJASN* Editor-in-Chief Rajnish Mehrotra, MBBS, MD, FASN, and the winners of the 2016 ASN Innovations in Kidney Education Contest.

ASN Communities, Social Media

Every day, ASN Communities allow thousands of kidney health professionals to network, collaborate, and discuss issues facing the specialty on an online platform. ASN members from around the world composed approximately 12,000 posts across 13 communities led by 42 community leaders. Six new interest-based communities opened, providing venues for focused discussion on issues from public policy to women's health.

ASN's social media platforms show continued growth. Twitter followers for @ASNkidney grew by 20%, and followers of ASN's facebook page grew by 53%. Steady growth was also seen for @ASNadvocacy and @KidneyNews. ASN's social media users are mostly from the United States, the United Kingdom, Mexico, Canada, Spain, and India.

Goal 2—Transform kidney research through discovery and innovation to prevent, treat, and cure kidney diseases

Innovation and Discovery Task Force

ASN launched the Innovation and Discovery Task Force. Chaired by S. Ananth Karumanchi, MD, the task force is charged with developing a recommendation for ASN to meet the second goal of its Strategic Plan: "Transform kidney research through discovery and innovation to prevent, treat, and cure kidney diseases." To meet its goals, the task force has assessed the current activities of ASN focused on fostering innovation, discovery, and research as well as studied the efforts of peer medical societies, patient organizations, foundations, and other exceptional innovators.

The task force identified the need to support and develop future innovators, communicate and educate clinicians regarding breakthrough treatments and approaches, and identify innovative mechanisms and funding sources to generate evidence for and success of cutting edge clinical research to prevent, treat, and cure kidney diseases.

Kidney Health Initiative (KHI)

A public-private partnership among ASN, the U.S. Food and Drug Administration, and the nephrology community, KHI now comprises over 80 organizations. KHI workgroups and the KHI Patient and Family Partnership Council advanced the mission of enhancing patient safety and stimulating innovation in kidney disease.

KHI's signature initiative, "Developing a Roadmap for Innovative Alternatives in Renal Replacement Therapy," completed its first phase—to identify technical challenges to mechanical and cellular technologies. KHI also published the article "Stimulating Patient Engagement in Medical Device Development in Kidney Disease: A Report of a Kidney Health Initiative Workshop" in the *American Journal of Kidney Diseases* and finalized two sets of data standards, "Diabetic Kidney Disease Therapeutic Area User Guide" and the "Kidney Transplant Therapeutic Area User Guide."

ASN Foundation for Kidney Research Grants

The ASN Foundation for Kidney Research provides more than $3 million in funding for clinical and basic research for members at all stages of their careers. The Foundation funded 39 leading researchers working to cure kidney diseases through 19 new projects and 20 projects continuing from work begun in 2016.

The Foundation funds the Career Development Grants Program, the Ben J. Lipps Research Fellowship Program, the William and Sandra Bennett Clinical Scholars Program, and the American Society of Nephrology–Harold Amos Medical Faculty Development Program. Beginning in 2018, the Foundation will award five fellowships per year to nephrology PhD students through the ASN Pre-Doctoral Fellowship Program.

Goal 3—Encourage every kidney health professional in the world to contribute to, and benefit from, ASN

ASN Expands Minority Research Award

The ASN-Harold Amos Medical Faculty Development Program (AMFDP) Award, formed in partnership with the Robert Wood Johnson Foundation, was expanded to include two scholars during any given award cycle. Aiming to address the shortage of minority scholars with academic and research appointments in nephology, the ASN-AMFDP program offers four-year postdoctoral research awards.

The first ASN-AMFDP recipient, Gentzon Hall, MD, PhD, of Duke University School of Medicine, has a research focus on novel gene discovery in African Americans with familial focal segmental glomerulosclerosis. Applications will open again during 2018 for a second scholar.

ASN Outreach at Student National Medical Association (SNMA)

ASN exhibited at the SNMA Annual Meeting in Atlanta, GA, and enrolled more than 60 students for ASN membership. ASN Diversity and Inclusion Committee members Robert S. Hoover, Jr., MD, FASN, and Dimitri A. Augustin, MD, attended the meeting and invited several Emory University faculty members and local practicing nephrologists to speak to students at the ASN booth.

ASN also hosted a reception attended by more than 100 students. The outreach is part of an initiative by the diversity and inclusion committee to increase interest in nephrology careers among students from backgrounds underrepresented in medicine.

Membership Satisfaction, Growth

ASN membership is more than 17,000, an increase over the previous year. Approximately 40% of members now come from outside the United States.

A survey of members asked for input on the value of ASN membership and benefits. More than 90% of respondents said ASN is a primary and reliable source for information on nephrology. One-half cited the ability to stay current about clinical information, trends, and regulatory changes in nephrology, as well as ASN publications, as primary reasons for joining and renewing membership. Members also identified conferences and events and the ability to network with one another as top benefits. When asked what they value most about ASN, members emphasized the credibility ASN provides within the profession.

Goal 4—Foster career development for current and future kidney health professionals

Securing the Future Campaign

The ASN Foundation for Kidney Research received a $1 million contribution from Keryx Biopharmaceuticals, Inc., to establish the Joseph V. Bonventre Career Development Grant, awarded every other year starting in 2018.

The Foundation's *Securing the Future Campaign* aims to endow the Career Development Grants Program, which has awarded $31,500,000 in support of talented investigators transitioning to independent research careers since 1996.

Nephrology Workforce Research, Data Efforts

Now in its second year, the ASN Data Analytics Program collaborated on multiple projects assessing educational needs in nephrology fellowship and factors influencing specialty choice. Initial data on Internal Medicine Residencies from the Best Practices Project will be presented at ASN Kidney Week 2017.

The program oversees the joint Comparing Realities Across the Global Nephrology Workforce project, a collaboration among ASN, ERA-EDTA, and ISN researchers to assess how nephrology practice varies across the world. ASN's new Nephrology GME Database allows researchers to monitor trends in the nephrology training landscape. A new Early Practice Survey targeted nephrologists 2 to 5 years out of fellowship training, providing a complement to the annual Nephrology Fellow Survey.

ASN Flash Polls assessed current perceptions about nephrology procedures among training program directors and division chiefs, informing discussions at this year's Nephrology Training Program Retreat. ASN will soon launch the ASN Data Resource Center, a dedicated online platform for ongoing nephrology workforce research.

ASN Launches Kidney TREKS in Chicago

To help spur interest in nephrology among trainees, ASN added a new site to the Kidney TREKS (Tutored Research and Education for Kidney Scholars) program. Now offered at both the University of Chicago and Mount Desert Island Biological Laboratory in Maine, Kidney TREKS offers selected medical students and PhD candidates a chance to explore nephrology through a weeklong kidney research and outreach course, long-term mentorship program, and opportunities for continued participation with ASN.

A preliminary assessment of the Kidney TREKS program found that among 48 participants for whom follow-up data were available, almost half had entered a pipeline specialty leading to nephrology (internal medicine, pediatrics, or medicine-pediatrics) or were conducting research in the kidney space. Of 40 medical student participants, 40% entered a relevant pipeline, and 78% of the researchers (graduate students, PhD candidates, and postdoctoral fellows) had published kidney-focused research.

ASN Travel Support

ASN provided students and trainees with four opportunities to attend Kidney Week 2017: the Advances in Research Conference (ARC) Early Program, the Karen L. Campbell, PhD, Travel Support Program for Fellows, the Kidney STARS (Students and Residents) Program, and the William E. Mitch, III, MD, FASN, International Scholars Travel Support Program.

A total of 389 students and trainees will participate in these travel support programs, including 269 Kidney STARS, 77 Campbell Fellows, 35 ARC Early Program attendees, and eight Mitch International Scholars.

Goal 5—Assert the value of nephrology to health and science professionals, health care systems, and other stakeholders to ensure high-quality care for patients

Nephrologists Transforming Dialysis Safety (NTDS)

The mission of ASN's partnership with the U.S. Centers for Disease Control and Prevention is to engage nephrologists as team leaders to target zero infections in dialysis facilities. NTDS developed strategies to enhance implementation of recommended infection prevention practices within the nephrology community.

Through a series of community meetings and focus group sessions, NTDS identified infection control challenges, barriers and opportunities to improve infection prevention practices, as well as methods for early detection and proper treatment of bacterial infections in patients undergoing dialysis. NTDS also used a needs assessment to develop the 2017 Roadmap that guides its work.

NTDS launched an educational webinar series with the first webinar entitled, "Targeting Zero Infections: Where Do We Begin?" The webinar addressed the virulence of hepatitis C and the role of the nephrologist as a leader in combating its spread. Webinar participants were directed to the online resource library, a key feature of the NTDS website. Six other webinars and educational offerings at ASN Kidney Week will follow.

A Voice on Capitol Hill

ASN partnered with 21 other health care organizations to advocate for kidney patients and professionals on Capitol Hill. Advocates met with lawmakers to urge dedicated kidney research funding for NIH of $150 million per year for 10 years and for passage of the Living Donor Protection Act on Kidney Health Advocacy Day in March and Kidney Community Advocacy Day in September.

Disaster Relief Efforts for Kidney Patients

To help provide continuity of care for displaced dialysis patients in need of treatment, ASN reacted swiftly following Hurricanes Harvey and Irma. ASN joined efforts by the American Kidney Fund (AKF), the Kidney Community Emergency Response Coalition, dialysis organizations, and other stakeholders to help kidney patients in the aftermath of these natural disasters.

ASN donated $20,000 to the relief efforts for dialysis patients coordinated by AKF to help replace medication, provide transportation to dialysis treatment, and cover household and food essentials. ASN also encouraged interested members to contribute to the AKF's Disaster Relief Program.

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

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

Policy Update

Kidney Advocates Urge NIH Funding Boost, Living Donor Protections

By Zachary Kribs

Advocates from the American Society of Nephrology (ASN) and 21 other kidney and transplant health care organizations met with nearly 100 members of Congress or their staff during the third perennial Kidney Community Advocacy Day on September 19, 2017 (Table 1). A total of 75 advocates urged Congress to continue its historic support of research funding for the National Institutes of Health (NIH) and to cosponsor and pass the Living Donor Protection Act (H.R. 1270), no-cost legislation that would eliminate barriers to living donation and increase access to transplants.

The Capitol Hill visits were part of an ongoing effort by ASN to bolster its legislative agenda. In March, advocates from ASN and the American Association of Kidney Patients met with members of Congress to advocate for increased research funding in the face of the administration's proposed budget cuts to the NIH, as well as to identify potential sponsors of the Living Donor Protection Act. Partly as a result of their efforts, Congress soundly rejected the administration's proposed NIH cuts, instead proposing an increase in funding in line with ASN's request, and has added nearly 30 co-sponsors to the Living Donor Protection Act. Kidney Community Advocacy Day expands on the progress made in previous efforts, with advocates calling on Congress to finalize the increase to the NIH budget and to pass the Living Donor Protection Act.

"The prevalence of kidney diseases in the U.S. is at a record high—I would even say rampant," said Crystal A. Gadegbeku, MD, chair of the ASN Policy and Advocacy Committee. "With a tremendous need for more innovation in kidney therapies coupled with a national organ shortage, we need Congress to move both to provide kidney-specific research funding, similar to the Special Diabetes Program, which has led to a Food and Drug Administration–approved artificial pancreas—and to take steps to eliminate barriers to donation by enacting the Living Donor Protection Act. This year's Government Accountability Office (GAO) report about the prevalence of kidney diseases in America and the underfunded state of kidney research should be both a wake-up call and a rallying cry for members of Congress and all Americans."

Funding for kidney research and elimination of barriers to living organ donation are highly important issues to the kidney care and transplant community. ASN rallied to support these two causes with the 21 other organizations on Kidney Community Advocacy Day to show unity in the kidney care and transplant community in the face of a challenging political climate and era of austerity for many federal budgets.

Report reveals disease burden, funding mismatch

In January, the U.S. Government Accountability Office released a report detailing that 17% of Americans (40 million) have kidney diseases and about 680,000 have kidney failure and rely on dialysis or a transplant to live. The GAO data show that Medicare spends nearly $33 billion on kidney failure, while the investment in federally funded kidney research is the equivalent of just about 1% of that amount. The United States Renal Data System (USRDS) data places total Medicare spending for all kidney diseases at $103 billion. In order to bring better value to Medicare and improve patient outcomes, patient and physician advocates urged Congress to support an additional $150 million per year over 10 years to establish a Special Statutory Funding Program for Kidney Research at The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), supplementing regularly appropriated funds the agency currently receives.

Advocates also asked Congress to pass the Living Donor Protection Act to remove barriers to living organ donation in order to address the nation's organ shortage crisis. Over 100,000 Americans are on the kidney transplant wait list. Although a patient is added to the list every 14 minutes, 13 Americans die every day waiting for a kidney transplant. Besides increasing quality of life, transplants also save Medicare expenditures compared to dialysis: Medicare spends about $30,000 per transplant patient versus nearly $90,000 per hemodialysis patient annually on average.

Participants in Kidney Community Advocacy Day represented a diverse group of kidney care and transplant physicians and patients, and traveled from 22 different states to speak to Congress about the importance of kidney research and living donation. Roughly 60% of these individuals had experienced a previous Kidney Community Advocacy Day. The night before, advocates gathered for a group dinner and training session during which staff from the represented organizations provided guidance on effective Capitol Hill advocacy and answered questions about the current political climate and its effect on kidney and transplant issues.

During the day, advocates shared their own personal experiences with kidney diseases with their congressional delegations. They cited these personal stories, as well as the high prevalence and large human toll of kidney diseases, as reasons for their involvement in advocating for more research funding and better care. After the event, participants urged others to get involved in advocacy, and many pledged to participate in a future Kidney Community Advocacy Day.

Left to right: Hon. Karen Thurman (a former congressional representative from Florida representing the PKD Foundation), Edward Drake II (Georgia, American Association of Kidney Patients), and John Menendez (Florida, Alport Syndrome Foundation), meet with a staff member from the office of Sen. David Perdue (R-GA).

Table 1. Participants in Kidney Community Advocacy Day 2017

Alport Syndrome Foundation
American Association of Kidney Patients
American Kidney Fund
American Nephrologists of Indian Origin
American Nephrology Nurses Association
American Society of Nephrology
American Society of Pediatric Nephrology
American Society of Transplantation
American Society of Transplant Surgeons
Children's Organ Transplant Association
Home Dialyzors United
IgA Nephropathy Foundation of America
Lowe Syndrome Association
NATCO
National Kidney Foundation
National Renal Administrators Association
NephCure Kidney International
Polycystic Kidney Disease Foundation
Renal Pathology Society
Renal Physicians Association
Society for Transplant Social Workers
Transplant Recipients International Organization

THE MORE

DIFFICULT THE CASE,

THE LESS DIFFICULT THE CHOICE OF HOSPITAL.

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Ranked No. 10 in the nation by *U.S. News & World Report,* 2017-18, our physicians and scientists at The Mount Sinai Hospital's Division of Nephrology are internationally recognized as authorities on the causes and treatments of all forms of adult and pediatric kidney diseases. Our kidney transplant specialists are investigating new ways to detect, prevent, and treat rejection that will have a lasting impact on the field. Our physicians are all on the faculty at the Icahn School of Medicine at Mount Sinai, which is ranked among the nation's top medical schools by *U.S. News & World Report.*

- Division of Nephrology
- Division of Pediatric Nephrology
- The Recanati/Miller Transplantation Institute
- Hypertension Program
- Glomerular Disease Program
- Mount Sinai Home Dialysis Program
- Mount Sinai Kidney Center (Dialysis)
- Mount Sinai Kidney Stone Center

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Nephrology and Palliative Care

What are the barriers to palliative care for those with kidney diseases? How do I respond when my patient says they want to stop dialysis? These are among the questions addressed in the September 2017 special section on palliative care. We continue the discussion here, with articles on hospice access, integrating advance care planning into the care of patients with kidney diseases and kidney failure, and nephrologists' attitudes toward palliative care.

Access to Hospice

By Debra Hain

An aging ESRD population with complex medical issues demands our attention. As nephrologists, we must seek to discover the best ways to achieve quality care and quality of life for these individuals and their families within a cost-constrained health care environment.

Older adults with ESRD have the option of withholding dialysis or withdrawing from dialysis when the burden outweighs the potential benefits. In these situations hospice care is one intervention that supports quality care, quality of life, and reduced health care costs through symptom management, spiritual and psychosocial support, and avoidance of unnecessary hospitalizations. Hospice care, however, continues to be underutilized owing to several barriers such as lack of education in hospice care and ineffective training regarding advance care planning that includes preferences for end-of-life (EOL) care (1, 2). The percentage of Medicare beneficiaries receiving hospice care at the time of death has increased over the past decade, but opportunities for improvement in EOL care remain, including improvement in timely referral for hospice care.

As supported by epidemiological data, most patients receive hospice services only after discontinuing dialysis treatments. From 2004 to 2013, use of hospice care increased from 59% to 82% in those discontinuing dialysis and from 5% to 8% among those who did not discontinue dialysis (3). Evidence has indicated that many individuals with ESRD die in the hospital, which is not only costly but often is incongruent with the person's wishes for EOL care. Advance care planning, in which health care professionals, patients, and families engage in shared decision-making that considers what matters most to the person living with ESRD, can facilitate greater hospice utilization and avoid costly hospitalization (4). Initiating hospice care earlier may allow death to occur in the person's place of choice.

Medicare hospice criteria

The four criteria for enrollment in Medicare Part A Hospice care are:

1. US citizen who is eligible for Social Security or railroad retirement benefits and over age 65 or under 65 years and eligible for Medicare because of a long-term disability for >2 years and/or ESRD,
2. referral to certified Medicare provider (generally certified by CMS to provide services under the Medicare hospice benefit),
3. a statement signed by patient stating they are choosing hospice care instead of regular Medicare for the terminal diagnosis (Medicare does allow for regular reimbursement for incidental medical expenses unrelated to terminal diagnosis; the relatedness is determined by hospice medical director), and
4. certification by the individual's personal physician and the hospice medical director that the person has a terminal diagnosis and with a life expectancy of six months or less if the illness takes its normal course. The patient's treatment goals should emphasize symptom management, and outcomes should focus on comfort and quality of life.

The Medicare Hospice Benefit is divided into a number of certification periods with eligibility for two 90-day periods followed by unlimited periods of 60 days. The person on hospice requires recertification at each of these timeframes to determine continued eligibility. An important criterion for recertification is continued decline. Since 2011, Medicare has required a face-to-face encounter by a physician or nurse practitioner prior to recertification period. Acute inpatient hospice care can be provided in a hospice facility for those who are actively dying or for complex symptom management that cannot be addressed in the home.

Medicare hospice benefit specific for ESRD

Unless individuals with ESRD have another terminal illness (e.g., cancer, chronic obstructive pulmonary disease, heart failure) that meets hospice criteria as determined by the hospice physician, they will have to forgo life-sustaining treatment related to ESRD (e.g., dialysis or transplantation). For example, if individuals have a terminal diagnosis of cancer that meets the Medicare Hospice Benefit criteria they can opt to continue the dialysis Medicare ESRD benefit. If the terminal diagnosis is kidney failure and dialysis is provided then it becomes the responsibility of the hospice provider to pay for the dialysis treatments. This really is not feasible because hospice providers are not reimbursed for the dialysis treatments and therefore, may not be able to financially encompass the high cost of providing this service (Table 1). However, it is important to contact the hospice organization because there is variability in the services each organization provides. Some hospice organizations have more flexible services or may receive charitable donations that can be designated for services that aren't included in the Medicare Hospice Benefit (2).

Another important issue to consider is that many patients may not understand that after being enrolled in hospice, they can revoke hospice, return to dialysis, and still receive the Medicare ESRD benefit. Considering that the life expectancy after withdrawing from dialysis is about 7 days, this decision may not happen before death occurs. The Coalition for Supportive Care of Kidney Patients (CSCKP) has developed a flowchart, Medicare Hospice Benefit & ESRD Patients, that can support health care professionals to assess if, and when, an individual may meet criteria for Medicare Hospice benefit. The flowchart is available at www.kidneysupportivecare.org.

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Table 1. CMS hospice criteria, benefits, and eligibility

CMS hospice criteria for kidney failure as a terminal diagnosis	CMS hospice benefits and eligibility specific for kidney failure
• Serum creatinine 8 mg/dL or greater (6 mg/dL or greater in patients with diabetes) or • Creatinine clearance <10 mL/min/1.73 m^2 (<15 mL/min/1.73 m^2 for individuals with diabetes) or • Symptoms	Home Health and Hospice Benefits Available for ESRD Beneficiaries, tagline 50.6.1. • "Medicare beneficiaries can receive care under both ESRD benefit and the home health or hospice benefits. The key is whether or not the services are related to ESRD." • "If the patient's terminal condition is not related to ESRD, the patient may receive covered services under both ESRD benefit and the hospice benefit. A patient does not need to stop dialysis treatment to receive care under the hospice benefit."

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"I Realized It Was Kind of Too Late"

Integrating Advance Care Planning into the Care of Patients with Kidney Disease

By Dale Lupu, MPH, PhD; Alvin H. Moss, MD; Nancy Armistead, MPA; and Brandy Vinson

"There's no doubt that my wife and I waited too long to have that discussion, and part of that is—my wife is very quiet … we've been married for 55 years. So we never really had that discussion. And before I realized, it was kind of too late." (interview 6, man, health care proxy for patient with cognitive impairment) (1).

"I think that discussion should come before you get to the critical point. At the jump of a dime things could turn, so I think the more prepared you are, the better you could handle things when situations get tough." (interview 1, family, woman) (1).

Patient and caregiver perspectives on advance care planning

In numerous studies, patients with chronic kidney disease (CKD) and ESRD have indicated that they want to talk about advance care planning (ACP) with their nephrologist and care teams (1, 2). ACP discussions are associated with improved goal-consistent care, including increased likelihood of dying in the patient's preferred setting, reduced hospitalization, and less aggressive care at the end of life (3, 4). Yet only 6% to 38% of dialysis patients have an advance care plan (5). Even when ACP is documented in the dialysis patient's medical record, it rarely documents specific patient preferences regarding dialysis. A study of Mayo Clinic dialysis patients found that only one half (49%) of the patients had a documented advance directive in their chart. Of these, only 10.6% of documents specifically mentioned patient preferences regarding dialysis, and less than one half (44.2%) addressed preferences for cardiopulmonary resuscitation (CPR) (6).

If this were merely a matter of getting more people to file paperwork, it might not be alarming. However, the low rates of ACP go hand in hand with evidence that patient preferences are not routinely elicited and followed. Davison (7) found that only 10% of patients reported an end-of-life care conversation with their nephrologist, despite the fact that such conversations were patients' highest priority in end-of-life planning (8).

Barriers to ACP for CKD and ESRD patients

Leaders in nephrology have advocated for more widespread integration of ACP into care (9), but many barriers have slowed progress. Providers often do not feel this is their job, many do not adequately understand ACP, and there is a lack of integration of multidisciplinary resources that could help (10, 11). Furthermore, many implementation details—such as the best timing, setting, and team—have not been well researched, leaving providers to experiment on their own.

A 2015 editorial on ACP for nephrology patients explicitly called for studies of earlier ACP before choosing dialysis, with particular attention to the concerns of patients choosing supportive care (2). The editorial also called for studies that illuminate implementation, stating "[t]he nephrology community would benefit greatly from well conducted clinical studies of the implementation and effectiveness of advance care planning programs. It is time to stop discussing the need for such clinical processes and to start exploring ways to make it work" (2).

Recent systematic reviews have synthesized current knowledge about ACP (12). Through two decades of research, we have learned that multimodal interventions that treat ACP as an ongoing process involving two-way communication are usually more effective than a narrow focus on forms to be completed. We have also learned that family members often do not know what patients prefer, even when they are the designated decision-maker; that patients and family members prefer earlier communication; that ACP does not have a detrimental effect on distress or anxiety; that certain interventions are effective in improving the match between patient preferences and care received; and that certain interventions are associated with cost-savings, although true cost-effectiveness has not been studied.

ACP resources from the Coalition for Supportive Care of Kidney Patients

To help address the need for ACP tools specific to nephrology settings, the Coalition for Supportive Care of Kidney Patients (CSCKP) has developed two patient brochures: one for patients before a dialysis decision and one for patients already on dialysis. A guide for staff to use in conducting an ACP discussion using motivational interviewing techniques complements the patient brochures.

The CSCKP approach to ACP is to normalize the process by decoupling it from worsening prognosis. The CSCKP suggests that everyone—especially those with a chronic disease—should have an advance care plan that specifies who should be called on to make medical decisions if the patient is unable to make them for herself and gives some guidance as to the principles to follow in making those decisions. The CSCKP advises patients to follow five steps:

1) Choose someone to make health care decisions for you if you get sick and cannot speak for yourself.
2) Think about what kind of health care you would want if you were unlikely to get better. Discuss your wishes with your family and friends.
3) Write your wishes down in a legal form known as an advance directive (sometimes called a living will or a medical power of attorney).
4) Give a copy of your advance directive to your health care agent and your kidney care team. Continue talking to your family about your wishes.
5) Work with your kidney care team to complete a medical order form (usually called POLST, MOLST, or POST; polst.org) to record your wishes.

Ideally, ACP is one part of ongoing discussions that the nephrology team initiates about the issues that arise in serious illness and is integrated into the workflow for the nephrology clinic or dialysis center (13). Table 1 shows common barriers to routine ACP and suggests resources or steps that a practice can take to improve its processes.

The nephrology community recognizes that successfully implementing ACP for CKD and ESRD patients is necessary to provide individualized patient-centered care. Multiple studies are underway to develop best practices for ACP for this patient population.

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Table 1

Barrier	Solution	Resources
Providers uncertain about how to discuss ACP	Use a conversation guide; enhance provider communication skills.	CSCKP ACP curriculum (kidneysupportivecare.org); VitalTalk training online (www.vitaltalk.org); Serious Illness Conversation Guide (https://www.ariadnelabs.org/areas-of-work/serious-illness-care/resources/#Downloads& Tools)
Uncertainty over who should initiate ACP—nephrologist? Primary care provider? Patient?	Commit to taking the lead.	See CSCKP resources for professionals (http://www.kidneysupportivecare.org/For-Professionals/Advance-Care-Planning.aspx)
Uncertainty over which patients are appropriate and when	Use an opt-out standard—assume that all patients should be offered ACP unless there is a specific contraindication.	
Need educational materials and forms for patients	Multiple resources now available; review and select the one that best suits your practice and patients.	Prepare for your care (https://www.prepareforyourcare.org/page); recognized forms in all states (www.caringinfo.org/i4a/pages/index.cfm?pageid=328); additional resources (www.kidneysupportivecare.org/For-Patients-Families/Advance-Care-Planning.aspx)
Time crunch for nephrologist	Involve other team members, such as nurse practitioners, social workers, or other trained coaches.	American Nephrology Nurses Association's "Techniques to Facilitate Discussions for Advance Care Planning (ACP)" module is the first in a series of educational modules on EOL decision-making, and the Nephrology Nurse is an in-depth national program to promote education for nurses and improve end-of-life care
Not part of regular workflow of clinic	Develop a standard process; make it a standing agenda item at QAPI meetings.	The CSCKP has a model Advance Care Planning Policy template to assist dialysis facility staff in developing ACP policies and procedures (http://www.kidneysupportivecare.org/For-Professionals/Advance-Care-Planning.aspx)
Not integrated within EMR	Use a template within the EMR that captures key data, including proxy contact information and content of discussions about patient values and preferences; train all staff so that ACP discussions are consistently documented in the same location.	Most EMRs have a place where advance directives can be stored; use the EMR capacity and improve on it with custom fields; however, make sure everyone knows how to use it, what information needs to be documented, and where to find the information when needed
ACP documents information not shared across settings	Participate in the POLST registry if your state has one; participate in other registries as available; if no local registry, make sure that ACP information is conveyed routinely to other providers along with information, such as laboratory values; help patients recognize the importance of keeping documents accessible.	POLST programs by state (http://polst.org/programs-in-your-state/)
This all takes time, which is costly	Appropriately code ACP sessions to receive Medicare reimbursement for ACP.	https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/FAQ-Advance-Care-Planning.pdf
Do not know whether ACP is making improvements	Adopt quality measures and conduct performance improvement projects for ACP.	Measuring What Matters—measures 7 to 9 (http://aahpm.org/quality/measuring-what-matters); additional suggestions in the work by Mandel et al. (13)

Abbreviations: ACP = advance care planning; CSCKP = Coalition for Supportive Care of Kidney Patients; EMR = electronic medical record; EOL = end of life; POLST = Physician's Orders for Life-Sustaining Treatment; QAPI = Quality Assurance & Performance Improvement.

Integrating Geriatrics into Nephrology: A Report on the 2017 American Geriatric Society Annual Scientific Meeting

By Rasheeda Hall, MD

The US dialysis population is growing faster than the number of new nephrologists. At the same time, our population is aging, and there is a shortage of geriatricians. Beyond efforts to expand the nephrology and geriatrics workforces, it is also extremely important to pursue interdisciplinary collaboration. How can we ensure that older adults receiving dialysis receive quality care for their geriatric conditions? How can geriatricians be great partners in managing older adults with chronic kidney disease? Communication between nephrologists and geriatricians will add value for patient care and generate ideas for research.

As the liaison between the American Society of Nephrology (ASN) and the American Geriatric Society (AGS), I attended the AGS annual meeting in May 2017. The meeting focused on current issues in aging and was geared toward all health care professionals who care for older adults, including nephrologists. The value of individualized care for older adults on the basis of life expectancy prediction was the focus of a compelling talk by Sei Lee of the University of California, San Francisco Department of Medicine, Division of Geriatrics. Patients predicted to have limited life expectancy are not likely to benefit from preventive interventions, such as colon cancer screening, Lee noted. This theme overlapped with my own presentation showing that the cost-effectiveness of arteriovenous fistula is reduced in older adults with limited life expectancy.

Beyond life expectancy, another key theme at the meeting was co-management. A poster from Laura Fernandez and Julie Paik at the Boston Veterans Affairs Medical Center highlighted a Geriatric-Nephrology Collaborative Clinic, in which a geriatrician performed comprehensive geriatric assessments in older veterans with chronic kidney disease. The geriatrician then identified geriatric syndromes and provided treatment recommendations to the nephrology team. Although functional impairment was the most common geriatric syndrome, the most common treatment recommendations were medication changes followed by referrals to nonphysician services, such as rehabilitation or audiology.

Laura Plantinga and her colleagues at Emory University presented a study about the association of serious fall injuries in dialysis patients who received a kidney transplant. They found that patients who experienced a serious fall injury were nearly 80% less likely to be waitlisted. Among the waitlisted patients, those who had a serious fall injury were 53% less likely to subsequently receive a transplant. Prior studies show that falls increase mortality risk in dialysis patients, so these findings bring attention to yet another complication of injurious falls in this population.

Another highlight from the AGS annual meeting is its annual morning meeting for medical subspecialists. As ASN liaison, I highlighted the ASN's Supportive Care online community and the Coalition for the Supportive Care of Kidney Patients Luncheon held at Kidney Week 2016. I also described current National Institute on Aging–funded research involving frailty, disability, and shared decision-making in older adults with ESRD. From other subspecialists' presentations, I learned about integrated working groups, such as the Cancer and Aging Research Group that pursues research collaborations across multiple institutions. This model of collaboration among various specialists at multiple institutions is an intriguing example for growing the field of geriatric nephrology.

Want to learn more and/or get involved in geriatric nephrology? Through the ASN's website, you can access the Online Curriculum on Geriatric Nephrology and the Supportive Care online community. At ASN Kidney Week 2017, you may network with members of the Supportive Care online community who will be present for a Supportive Care Meetup at the ASN Communities Lounge. Last, consider attending the next AGS annual meeting May 3 to 5, 2018, in Orlando, FL.

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Nephrologists' Interactions and Attitudes toward Palliative Care, End of Life

By Areeba Jawed

"Can I stop dialysis?" asked my 88-year-old wheelchair-bound patient on a late fall afternoon. I squinted my eyes to block not only the streaming sunlight but my reaction: one of bewilderment.

In a 2015 study of nephrology fellows, 99% of respondents agreed that physicians have a responsibility to help patients at the end of life (EOL) and in preparing for death; however, in their fellowship training, less than one-half were taught how to respond to a patient's request to discontinue dialysis therapy, conduct a family meeting about dialysis options, or determine when to refer patients to hospice or palliative care (1). As per the US Renal Data System, patients older than 75 years are the fastest growing dialysis population (2), and among the elderly with acute kidney injury who need dialysis, studies show that 50% or more die within the hospitalization (3). Now, more than ever, nephrologists face the question of EOL care in patients with chronic kidney disease and encounter the need for shared decision-making in the intensive care unit (ICU) when offering acute dialysis to the elderly with poor prognosis.

Patients on dialysis have a remarkably low rate of documented EOL preferences, despite known high mortality rates and evidence supporting that advance care planning (ACP) improves EOL care (4). Compared with cancer or congestive heart failure patients, ESRD patients are far more likely to be admitted to the ICU and much less likely to be enrolled in hospice in the last month of life, demonstrating the need for increased use of palliative resources by the nephrology community (5). It is particularly disappointing to see patients with ESRD do so poorly compared with others with chronic illnesses in this regard while there exists an environment conducive to eliciting patients' preferences given the frequent interaction with dialysis providers three times per week and continuity of care that may last for years.

Many reasons may account for the current attitude of nephrologists toward ACP and the suboptimal utilization of palliative care resources for dialysis patients. In a qualitative study undertaken to evaluate provider perspectives regarding ACP and to identify system-level barriers for its provision, four overlapping themes emerged that focused on the complex and fragmented nature of ESRD care, the lack of understanding of ACP by providers, the unclear locus of responsibility for ACP, and a dearth of active collaboration and communication among different providers of the same patients (6).

Most dialysis patients welcome discussions regarding prognosis and EOL preferences; however, they report a lack of initiation of such conversations by providers (4). These attitudes may be explained by multiple reasons: lack of time, discomfort experienced by clinicians when approaching EOL issues, clinicians not viewing it as their responsibility, and the uncertainty associated with communicating prognosis owing to a lack of reliable prognostication tools to help guide clinical decision-making. There is little emphasis during clinical training on providing learners with a skill set for effective conversations about serious illnesses (1); however, more recently, communication skills models for learning have been developed, such as Nephrotalk, and various prognostication tools are available (7, 8).

Lack of knowledge among providers and patients regarding palliative care and hospice options further limits their use. In a survey study from Europe representing 45 countries, the majority of nephrologists stated that their core curriculum did not include palliative care. Additionally, they had not attended continuous medical education sessions on this topic (9).

Current metrics to assess delivery of standard of care in dialysis patients focus on disease-specific parameters and leave little room to recognize the need and reward of the provision of palliative care to reduce symptom burden in patients. In fact, nephrologists in the United States identified financial incentives for dialysis as a potential barrier to withdrawal of dialysis therapy when warranted; this was compounded by lack of compensation for lengthy EOL care discussions with patients and families (10). Electronic health records can also facilitate or hinder the job of the nephrologist in ACP depending on how well the interface interacts with multiple providers; instances have been described where patients reportedly had conversations with primary care providers (PCPs) regarding EOL care that were not communicated to nephrologists by the patient or the PCP (11).

Patients on dialysis have multiple comorbidities, high symptom burden, and mortality approaching those for certain malignancies. There is a well recognized need for subspecialist palliative care skills in the nephrology world. Efforts need to be made to incorporate palliative care education within the nephrology curriculum for trainees, and system-level barriers should be addressed to facilitate provision of appropriate EOL care to dialysis patients. Nephrologists must advocate for the rights of their patients to live the life that they desire, because "… in stories, endings matter" (12).

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FGF23 Doesn't Predict Outcomes in Patients with Low-Risk Stage 3 CKD, Study Finds

In primary care patients with stage 3 chronic kidney disease (CKD), low vitamin D and high parathyroid hormone (PTH) are predictors of increased mortality—but high fibroblast growth factor 23 (FGF23) is not, reports a study in *BMJ Open*.

Vitamin D deficiency, PTH, and elevated fibroblast growth factor 23 (FGF23) have all been associated with increased mortality in individuals with chronic kidney disease (CKD).

Noting that previous studies focused only on the effects of FGF23 in relatively advanced CKD, Adam Shardlow, of the Royal Derby Hospital Renal Medicine Department, and his colleagues set out to determine whether FGF23 is also a risk factor in people with early CKD, and to assess how this risk compares to the risk associated with vitamin D deficiency or elevated PTH.

Shardlow and his colleagues conducted a prospective cohort study of 1664 patients meeting KDIGO criteria for stage 3 CKD, drawn from 32 UK general practices. Participants were predominantly older, with a mean age of 73 years, and had a low risk of progression of their kidney disease. About 60% of patients were women. Fibroblast growth factor 23, PTH, and vitamin D were evaluated as risk factors for mortality or for CKD progression over 5 years of follow-up.

At baseline, 29% of patients had elevated FGF23 (> 51 pg/mL). Twenty-five percent of patients had elevated PTH (> 65 pg/mL), 6.3% had vitamin D deficiency, and 38.9% had vitamin D insufficiency. During follow-up, 18.9% of patients died from any cause, and 17.4% had progression of CKD.

Mortality was higher for patients with elevated FGF23, elevated PTH, and vitamin D deficiency and insufficiency. In adjusted analyses, vitamin D deficiency and elevated PTH remained significant risk factors for mortality, with a hazard ratio of 1.62 and 1.42, respectively.

In contrast, FGF23 was not an independent predictor of death on multivariable analysis. None of the three markers was significantly associated with risk of CKD progression. Few patients in the primary care sample had progression to end stage renal disease.

"While FGF23 may have a role as a risk marker in high-risk populations managed in secondary care, our data suggest that it may not be as important in CKD stage 3, managed in primary care," the authors write.

Shardlow A, et al. Associations of fibroblast growth factor 23, vitamin D and parathyroid hormone with 5-year outcomes in a prospective primary care cohort of people with chronic kidney disease stage 3. *BMJ Open*. 2017; http://dx.doi.org/10.1136/bmjopen-2017-016528].

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> **I was transitioning from a fellow to a faculty position. The award gave me protected time to start developing.**
>
> Rulan S. Parekh, MD, FASN
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> **ASN threw me a lifeline that allowed me to continue when there wasn't federal funding available.**
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> **The work that I've been able to accomplish was derived directly from the support of a Career Development Grant.**
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For adult patients with chronic gout refractory to conventional treatments to address their significant urate burden

OPEN THEM TO THE POSSIBILITY OF COMPLETE RESOLUTION IN MONTHS, NOT YEARS[1]

In the pivotal clinical trials for KRYSTEXXA® (pegloticase)

42% **of patients** had a complete serum uric acid (sUA) response and met the primary endpoint of maintaining sUA <6 mg/dL for ≥80% of the time in months 3 and 6[2,3]*

45% **of patients** had complete resolution of at least 1 target tophus, with no new or progressive tophi, in 6 months[1]*

*Based on the pooled results of replicate, multicenter, randomized, double-blind, placebo-controlled 6-month trials. Patients included adults with chronic gout refractory to conventional therapy. All investigators and patients were blinded to both treatment arm and sUA response.[1,3]

Patients with comorbid chronic kidney disease experienced similar efficacy and safety compared with the rest of the patient population.[3,4]

Not an actual depiction of chronic refractory gout.

INDICATIONS AND USAGE

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.

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

IMPORTANT SAFETY INFORMATION

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS

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-type hypersensitivity reactions have also been reported. KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions. Patients should be premedicated with antihistamines and corticosteroids. Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA. Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.

The risk of anaphylaxis and infusion reactions is higher in patients who have lost therapeutic response.

Concomitant use of KRYSTEXXA and oral urate-lowering agents may blunt the rise of sUA levels. Patients should discontinue oral urate-lowering agents and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

In the event of anaphylaxis or infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate.

Inform patients of the symptoms and signs of anaphylaxis, and instruct them to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.

CONTRAINDICATIONS: G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

Screen patients for G6PD deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. Do not administer KRYSTEXXA to these patients.

To learn more about the clinical benefits of KRYSTEXXA, VISIT BOOTH 910

www.KRYSTEXXAhcp.com

GOUT FLARES

An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including treatment with KRYSTEXXA. If a gout flare occurs during treatment, KRYSTEXXA need not be discontinued. 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 studied in patients with congestive heart failure, but some patients in the clinical trials experienced exacerbation. Exercise caution when using KRYSTEXXA in patients who have congestive heart failure and monitor patients closely following infusion.

ADVERSE REACTIONS

The most commonly reported adverse reactions in clinical trials with KRYSTEXXA are gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.

To report SUSPECTED ADVERSE REACTIONS, contact Horizon Pharma Rheumatology LLC at 1-866-479-6742 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see brief summary of Prescribing Information, including Boxed Warning, on following pages.

References: 1. Baraf HS, Becker MA, Gutierrez-Urena SR, et al. *Arthritis Res Ther*. 2013;15(5):R137. **2.** Sundy JS, Baraf HSB, Yood RA, et al. *JAMA*. 2011;306(7):711-720. **3.** KRYSTEXXA [prescribing information]. Horizon Pharma Rheumatology LLC. September 2016. **4.** Yood RA, Ottery FD, Irish W, Wolfson M. *BMC Res Notes*. 2014;7:54. doi:10.1186/1756-0500-7-54.

KRYSTEXXA® pegloticase

HORIZON PHARMA

KRYSTEXXA® (pegloticase injection), for intravenous infusion
Initial U.S. Approval: 2010

Brief Summary of 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 (5.1, 5.2).**
- **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.**
- **KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.**
- **Patients should be pre-medicated with antihistamines and corticosteroids.**
- **Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA.**
- **Monitor serum uric acid levels prior to infusions and consider discontinuing 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. Do not administer KRYSTEXXA to patients with G6PD deficiency (4, 5.3).**

INDICATIONS AND USAGE

KRYSTEXXA® (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

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

CONTRAINDICATIONS

Glucose-6-phosphate dehydrogenase (G6PD) deficiency

WARNINGS AND PRECAUTIONS

Anaphylaxis

During pre-marketing controlled clinical trials, anaphylaxis was reported with a frequency of 6.5% of patients treated with KRYSTEXXA every 2 weeks, compared to none with placebo. Manifestations included wheezing, peri-oral or lingual edema, or hemodynamic instability, with or without rash or urticaria. 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. [*See Adverse Reactions* (6), in full prescribing information]

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 consider discontinuing 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

During pre-marketing controlled clinical trials, 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. [*See Adverse Reactions* (6), in full prescribing information]

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 consider discontinuing 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* (4), in full prescribing information] 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

Gout flares may occur after initiation of KRYSTEXXA. [*see Adverse Reactions* (6.1), in full prescribing information] 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* (2), in full prescribing information]

Congestive Heart Failure

KRYSTEXXA has not been formally studied in patients with congestive heart failure, but some patients in the clinical trials experienced exacerbation. [*see Adverse Reactions* (6.1), in full prescribing information] 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* (6.2), in full prescribing information]

ADVERSE REACTIONS

The most commonly reported adverse reactions that occurred in greater than or equal to 5% of patients treated with KRYSTEXXA 8mg every 2 weeks are provided in Table 1.

Table 1. Adverse Reactions Occurring in 5% or More of Patients Treated with KRYSTEXXA Compared to Placebo

Adverse Reaction (Preferred Term)	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).

All patients in pre-marketing controlled clinical trials were pre-treated with an oral antihistamine, intravenous corticosteroid and/or acetaminophen to prevent anaphylaxis and infusion reaction. Patients also received non-steroidal anti-inflammatory drugs or colchicine, or both, for at least 7 days as gout flare prophylaxis before beginning KRYSTEXXA treatment. [*see Boxed Warning, Warnings and Precautions* (5.1, 5.2, 5.4), in full prescribing information]

Immunogenicity
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.

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.

USE IN SPECIFIC POPULATIONS

Pregnancy Category C
There are no adequate and well-controlled studies of KRYSTEXXA in pregnant women. KRYSTEXXA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Pegloticase was not teratogenic in rats and rabbits at approximately 50 and 75 times the maximum recommended human dose (MRHD), respectively (on a mg/m^2 basis at maternal doses up to 40 and 30 mg/kg twice weekly, in rats and rabbits, respectively). Statistically significant decreases in mean fetal and pup body weights were observed at approximately 50 and 75 times the MRHD respectively (on a mg/m^2 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/m^2 basis at maternal doses up to 10 mg/kg twice weekly in both species).

Nursing Mothers
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. 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.

PATIENT COUNSELING INFORMATION

See Medication Guide

General Information
Provide and instruct patients to read the accompanying Medication Guide before starting treatment and before each subsequent treatment.

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.
- 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* (5.1, 5.2), *Adverse Reactions* (6.1), in full prescribing information]
- 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* (5.3), *Contraindications* (4), in full prescribing information]

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* (5.4), *Adverse Reactions* (6.1), in full prescribing information] Advise patients that they should not stop KRYSTEXXA therapy if they have a flare.

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HORIZON PHARMA

KRYSTEXXA®
pegloticase

A Different Direction in SHPT

Rayaldee® is the first and only extended-release prohormone of the active form of vitamin D_3 that raises 25-hydroxyvitamin D and lowers iPTH levels.

Indication and Limitations of Use

Rayaldee® (calcifediol) extended-release 30 mcg capsules is indicated for the treatment of secondary hyperparathyroidism in adults with stage 3 or 4 chronic kidney disease and serum total 25-hydroxyvitamin D levels less than 30 ng/mL. Rayaldee is not indicated in patients with stage 5 chronic kidney disease or end-stage renal disease on dialysis.

Important Safety Information

Hypercalcemia: Excessive administration of vitamin D compounds, including Rayaldee, can cause hypercalcemia and hypercalciuria. Severe hypercalcemia due to substantial overdosage of vitamin D and its metabolites may require emergency attention. Patients should be informed about the symptoms of elevated calcium. • Digitalis toxicity: Potentiated by hypercalcemia of any cause. Monitor serum calcium and signs and symptoms of digitalis toxicity more frequently when

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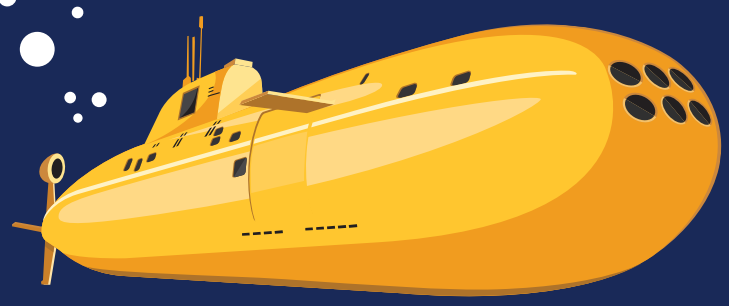

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initiating or adjusting the dose of Rayaldee. • Adynamic Bone Disease: Monitor for abnormally low levels of intact parathyroid hormone (iPTH) levels when using Rayaldee, and adjust dose if needed. • The most common adverse reactions (≥3% and more frequent than placebo) were anemia, nasopharyngitis, increased blood creatinine, dyspnea, cough, congestive heart failure and constipation. • Care should be taken while dosing Rayaldee with cytochrome P450 inhibitors, thiazides, cholestyramine or drugs stimulating microsomal hydroxylation due to the potential for drug interactions. • Serum calcium should be below 9.8 mg/dL before initiating treatment. • Monitor serum calcium, phosphorus, 25-hydroxyvitamin D and iPTH 3 months after starting therapy or changing dose.

Please see Brief Summary of Prescribing Information on following page, and Full Prescribing Information at RAYALDEE.com.

OP-US-0182-082017v.1

IN MEMORIAM

Professor Kirpal Singh Chugh

December 12, 1932 – September 17, 2017

By Brian J. G. Pereira, MD, DM

The global nephrology community mourns the passing of Professor Kirpal Singh Chugh, fondly called the "Father of Indian Nephrology," on September 17, 2017. He was 85.

Dr. Chugh was a remarkable individual on every front. For over five decades, he was the driving force of nephrology in India, the Asia-Pacific region, and the international arena. After completing his medical education at Punjab University in India, he trained in the UK and returned to India to establish the Department of Nephrology at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, in 1965. In addition to establishing the first nephrology training program in South Asia, he led the formation of the Indian Society of Nephrology in 1970, and was instrumental in launching the *Indian Journal of Nephrology*.

Dr. Chugh was a teacher par excellence. His students came first, and he spared no time nor effort to ensure that every clinical, teaching, or research question raised had been answered in its entirety. More important, he inculcated a culture of excellence, global leadership, and high aspirations. Each year, he invited world leaders in nephrology to visit PGIMER and spend time with the fellows, to ignite high expectations and instill in them a responsibility to advance science and patient care. Over three decades, he trained over 75 fellows, many of whom went on to lead the premier nephrology departments in India and abroad. His trainees have also provided leadership at the highest levels of global nephrology societies, including as past and future Presidents of the National Kidney Foundation (NKF), International Society of Nephrology (ISN) and American Society of Nephrology (ASN). He is rightfully acknowledged as the Dronacharya of Nephrology, after the legendry teacher in the Indian epic Mahabharata.

A commitment to the advancement of nephrology in the developing world was one of Dr. Chugh's ardent passions. He helped set up nephrology societies in most South Asian countries, and was one of the founder-members of the Asian Pacific Society of Nephrology. An early leader in ISN, he was the first Indian to be elected to the ISN Council, served on several Committees, and was the first Chair of the South Asian Committee of the ISN COMGAN Program, a forerunner of the current Regional Boards. His distinctive turban and engaging personality made him a stand-out at global nephrology conferences. He received numerous awards, including the Padmashree, one of the highest civilian awards in India, the Bywaters Award of the International Society of Nephrology, the Oshima Award of the Asian Pacific Society of Nephrology, and the Distinguished Medal of the National Kidney Foundation of the US.

On the personal front, Dr. Chugh was disciplined, punctual, and industrious and instilled the same expectations in his trainees and colleagues. He was fiercely loyal to his trainees, opened many doors to them, and would leave no stone unturned to ensure his trainees got their due. He and his wife Harjeet set a high bar in affection and hospitality, a "Chugh Trait" that his trainees took along as they set up departments and institutions of their own. He knew and remembered the names of every spouse and every child of his trainees and kept close track of their own careers and personal progress. Dr. Chugh took charm and grace to the level of an art form.

Although no longer with us, Dr. Chugh's lasting legacy lives through generations of his trainees and their own trainees—"The Chugh Way" will endure!

Brian J. G. Pereira, MD, DM, is a 1988 graduate of the Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Book Review

Hundreds of Interlaced Fingers: A Kidney Doctor's Search for the Perfect Match

Hardcover, 261 pages, Amistad

By Vanessa Grubbs, MD

Reviewed by Glenda Payne, RN

The effect of disparity on kidney transplant

In *Hundreds of Interlaced Fingers: A Kidney Doctor's Search for the Perfect Match*, Dr. Vanessa Grubbs describes her personal journey from a primary care physician never really interested in nephrology to meeting and falling in love with a man on dialysis, to volunteering as a kidney donor, and finally, to deciding to specialize in nephrology. During this journey, she recognized the implicit racism that continues to exist in the medical community, where assumptions are made on the basis of preconceived ideas regarding ability to pay for medications, keep follow-up appointments, and understand the complex regimens required for success after transplantation.

This implicit racism shows up in slow referrals for transplantation (her husband waited a year for referral), delayed response to a surgical complication (a surgeon may have responded more urgently if the patient was not black), and continued beliefs that there are real biological differences in our "made-up race categories."

"This series of assumptions and shortcuts in medicine … (where) we use race as a diagnostic tool … restricts our thinking, making it lazy at best," Dr. Grubbs states. A broader concern expressed is that race-based generalizations are made and accepted as true with little to no evidence basis.

The title is an analogy to the similarities of an electron scanning micrograph of the structure of the glomerulus to hundreds of interlaced fingers. A primary reason Dr. Grubbs chose to specialize in nephrology was to focus on research topics to learn more about why racial disparity persists in transplantation. One proposal included looking at how many patients referred for transplant evaluation actually received transplants by race and how many people were involved in deciding who got kidney transplants by race. In addition to this quantitative research, she proposed a qualitative piece "to get at all the reasons why the numbers of who had kidney failure and who got kidney transplants didn't add up." Senior faculty thwarted this project as too controversial and an attempt to show the transplant system is racist. And maybe it is. As Dr. Grubbs states, "I probably would ask different research questions if I weren't black or had different experiences, which is the very reason why it is important to have people from different backgrounds doing research."

In 2007, Dr. Grubbs published an article, "Good for harvest, bad for planting" in *Health Affairs* (Millwood) (1). This article is more tightly focused on the disparities she noted in the distribution of donated kidneys. *Hundreds of Interlaced Fingers*, while including concerns about these racial disparities, also recognizes the effect of low health literacy on referral for transplant. Patients with low health literacy had an almost 80% lower likelihood of being referred for kidney transplant evaluation. Perhaps in response to this finding, sections of her book explain in layman's terms the decline of kidney function, how dialysis works, and the risks and stresses of dialysis.

Dr. Grubbs acknowledges the incremental improvement in racial disparities that can be attributed to the recent change in the deceased donor kidney allocation system, while pointing out the feelings engendered by their evaluation at the transplant center: "The message we took away was, 'The kidney transplant system doesn't like black people.'"

Here is the challenge posed by this book for the nephrology community: receiving a kidney transplant "has everything to do with if a person with advanced kidney disease knows they have advanced kidney disease and has access to a nephrologist who thinks they are a good candidate for transplant, and the nephrologist actually refers them—a cascade of requirements vulnerable to the effects of personal bias and racism at an institutional level." Step one in meeting this challenge is recognizing our own biases and taking deliberate steps to overcome them.

Kidney News Editorial Board member Glenda Payne, MS, RN, is Director of Clinical Services at Nephrology Clinical Solutions in Lisle, IL.

Reference

1. Grubbs V. Good for harvest, bad for planting. *Health Affairs* 2007; 26:232–237.

Industry Spotlight

Cancer Drug Findings

Bristol-Myers Squibb (New York, NY) announced in early September 2017 a successful phase 3 study of a combination therapy to improve overall survival in kidney cancer.

The company tested a combination of its drugs Opdivo (nivolumab) and Yervoy (ipilimumab), which demonstrated better overall survival rates than a standard-of-care drug (Pfizer's SUTENT (sunitinib malate) in previously untreated patients with advanced or metatstatic renal cell carcinoma.

Bristol-Myers Squibb said the study was stopped early after a reduction in tumor size was noted in patients as part of a planned interim analysis. The combination treatment did not improve progression-free survival, but the trial did reduce tumor size in patients. Analysts from Barclays, quoted by Reuters, said the trial "provides perhaps the most explicit evidence to date that progression-free survival may not be the best yardstick to measure the benefit of immunology-oncology drugs."

The cancer drug bosutinib (Bosulif), under development by Pfizer, with research headquarters in Groton, CT, slowed cyst growth in patients with autosomal dominant polycystic kidney disease (ADPKD), according to a phase 2 clinical trial.

The drug is a kinase inhibitor indicated for the treatment of adult patients with differing forms of chronic myelogenous leukemia (CML) who have resistance or intolerance to prior therapy, according to prescribing information for the drug.

After two years of treatment, the annual rate of kidney enlargement was reduced by 66% in patients taking bosutinib 200 mg/day versus placebo (1.63% versus 4.74% per year, p = 0.01), according to findings reported in the *Journal of the American Society of Nephrology* (*JASN* 2017; doi:10.1681/ASN.2016111232).

Patients who took bosutinib at 400 mg/day had an even higher reduction in the rate of enlargement versus placebo (1.29% versus 4.74% per year). According to a protocol amendment for the trial, doses for 24 patients who initially received bosutinib at 400 mg/day were later reduced to 200 mg/day. Gastrointestinal and liver-related side effects were most common, but overall toxicity was consistent with the profile in prior studies of bosutinib, and no new toxicities were identified.

Dialyzer News

B. Braun (Melsungen, Germany; US base, Bethlehem, PA), a manufacturer of dialysis equipment and disposables and other medical products, has launched a new dialyzer called the Diacap Pro. The filter device, which received FDA approval in late August 2017, uses a new type of fiber designed to improve dialysis dose.

The Diacap Pro fibers clear blood toxins like urea and creatinine, while retaining molecules like albumin, and comes in three sizes (1.3 m^2, 1.6 m^2, and 1.9 m^2) to address differing patient needs.

The new dialyzer was designed to fit with other B. Braun products, including the Dialog+ Hemodialysis System, Solcart bicarbonate cartridge, and the AQUAboss Water Treatment system.

Intensive BP Reduction Linked to Higher CKD Incidence

In patients with hypertension and chronic kidney disease (CKD), more-intensive blood pressure–lowering therapy is associated with lower mortality risk, concludes a meta-analysis in *JAMA Internal Medicine*.

A systematic review identified 30 randomized clinical trials comparing more-intensive versus less-intensive blood pressure control in adults with stage 3 to 5 CKD. Meta-analysis comprised mortality data from 18 trials including 15,924 participants with CKD, 1293 of whom died. Thirteen trials had two defined blood pressure targets; five studies compared blood pressure-lowering therapy with no treatment or placebo.

At baseline, systolic blood pressure was similar between groups: mean 148 mm Hg. Mean reductions in systolic blood pressure were 16 mm Hg in patients assigned to the more-intensive interventions versus 8 mm Hg in the less-intensive group.

Mortality was 7.8% in the more-intensive group versus 8.4% in the less-intensive group. The reduction in all-cause mortality was significant: odds ratio 0.86. There was no evidence of heterogeneity, and the results were similar in subgroup analyses, including exclusion of SPRINT.

This meta-analysis suggests a 14% reduction in all-cause mortality with more-intensive blood pressure-lowering therapy among patients with stage 3 to 5 CKD. The mortality benefit appeared larger in trials with greater reductions in systolic blood pressure, although this was not significant. While emphasizing the need for further studies and safety monitoring, the investigators conclude, "[T]hese data support that the net benefits may outweigh the net harms of more intensive BP lowering in persons with CKD" [Malhotra R, et al. Association between more intensive vs less intensive blood pressure lowering and risk of mortality in chronic kidney disease stages 3 to 5: a systematic review and meta-analysis. *JAMA Intern Med* 2017; DOI:10.1001/jamainternmed.2017.4377].

Industry Spotlight

Minimal Contrast Dye Product Development

Two companies with products that reduce the amount of contrast dye in a patient's system are raising money to increase sales and to support critical research. Contrast dye used in vascular and other imaging may cause such complications as acute kidney injury (AKI) in kidney-impaired patients.

Osprey Medical's (Minnetonka, MN) DyeVert PLUS, which received FDA marketing clearance in March 2017, allows for a minimization of contrast dose, contrast monitoring in real-time, and notification to physicians when limits based on kidney function are reached. A special syringe allows release of minimal dye needed, with recapture of the unused portion.

Osprey plans to expand its U.S. sales team, with a focus on regions with higher rates of AKI, and to begin a pilot sales program in Germany.

Milford, Massachusetts-based RenalGuard also aims to attract funding for a trial of its contrast dye product, reports Fierce Biotech, a pharmaceutical industry blog. The company raised $14.5 million in March.

RenalGuard Therapy works by inducing higher rates of urine than are possible with standard diuretics. RenalGuard achieves these urine rates by monitoring and matching a saline infusion rate to the patient's urine output milliliter-for-milliliter, minute-by-minute. The automated balancing reduces the risk of over- or under-hydration relative to standard infusion, the company reports. The device protects kidneys by increasing urine in order to flush out contrast dyes before they cause damage.

KIDNEY WEEK 2017

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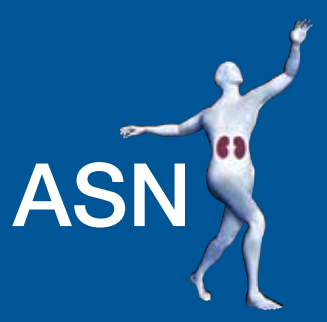


as of August 25, 2017

Plenary Session

Policy Analyst to Speak on Future of Health Care

Harold D. Miller

A nationally known health care reform expert will deliver the Christopher R. Blagg, MD, Lectureship in Renal Disease and Public Policy on Thursday, Nov. 2. Harold D. Miller will speak on "Creating a Physician-Led Health Care Future."

Miller is the president and CEO of the Center for Health Care Quality and Payment Reform, a national policy center. He is also adjunct professor of public policy and management at Carnegie Mellon University in Pittsburgh.

A nationally recognized expert on health care payment and delivery reform, Miller has worked in more than 40 states and metropolitan regions to help physicians, hospitals, employers, health plans, and government agencies design and implement changes. He assisted the Centers for Medicare & Medicaid Services with the implementation of its Comprehensive Primary Care Initiative in 2012. He has been invited twice to testify before Congress on how to reform health care payment. He is a member of the federal Physician-Focused Payment Model Technical Advisory Committee created by Congress to advise the secretary of health and human services on the creation of alternative payment models.

Miller has written many widely used papers and reports on health care payment and delivery reform, including "From Volume to Value: Better Ways to Pay for Healthcare," which appeared in the September 2009 issue of *Health Affairs*; "Win-Win-Win Approaches to Healthcare Cost Control Through Physician-Led Payment Reform," in the March 2014 *Clinical Gastroenterology and Hepatology*; and "Making Value-Based Payment Work for Academic Health Centers," in the journal *Academic Medicine*. He co-authored *A Guide to Physician-Focused Alternative Payment Models*, published in 2015 by the American Medical Association (AMA) and the Center for Healthcare Quality and Payment Reform. He wrote the AMA's 2010 report, Pathways for *Physician Success Under Healthcare Payment and Delivery Reforms* as well as the Massachusetts Hospital Association's 2009 report *Creating Accountable Care Organizations in Massachusetts*.

From 2008 to 2013, Miller served as president and CEO of the Network for Regional Healthcare Improvement, a national association of collaboratives. He was a member of the board of directors of the National Quality Forum from 2009 to 2015. From 2006 to 2010, he was a consultant to the Pittsburgh Regional Health Initiative. In 2007, he was the facilitator for a task force that prepared the recommendations for Minnesota's path-breaking health care reform legislation in 2008.

Miller has served as the director of the Pennsylvania Governor's Office of Policy Development, associate dean of the Heinz School of Public Policy and Management at Carnegie Mellon University, executive director of the western division of the Pennsylvania Economy League, director of the Southwestern Pennsylvania Growth Alliance, and president of the Allegheny Conference on Community Development.

State-of-the-Art Lecture

Pioneer in Tissue Bioengineering to Describe Dialysis Applications

Laura E. Niklason, MD, PhD

"Human-Engineered Tissues for Dialysis Access" is the title of a state-of-the-art lecture to be given on Thursday, Nov. 2.

The speaker will be Laura E. Niklason, MD, PhD, the Nicholas M. Greene Professor in Anesthesia and Biomedical Engineering at Yale University, where she has been on the faculty since 2006.

Dr. Niklason's research focuses primarily on regenerative strategies for cardiovascular and lung tissues, but the first use of the new technology is likely to be grafts for use in hemodialysis. Dr. Niklason's engineered blood vessels are currently in clinical trials, and are the first engineered tissues to be studied in a phase III trial. The approach does not require any cells from the patient; the engineered tissue is available "off-the-shelf."

Studies in vascular tissue mechanics showed several decades ago that most of the mechanical properties of arteries are derived not from the cellular components, but from the collagen- and elastin-based extracellular matrix. Using this principle, Dr. Niklason's research team utilized banked human vascular smooth muscle cells to engineer implantable arteries. In this process, they seed allogeneic vascular cells onto a degradable substrate to culture vascular tissues in a biomimetic bioreactor. After eight to 10 weeks, the engineered tissues are decellularized to produce an engineered extracellular matrix–based graft.

The advantage of using allogeneic cells for graft production is that no biopsy needs to be harvested from the patient, and no patient-specific culture time is required. The acellular grafts can be stored for six months and are available when patients need them.

These grafts have been tested most extensively for hemodialysis access in patients who are not candidates for autogenous arteriovenous fistula creation. The first patient was implanted in December 2012 in Poland. Since then, 60 patients have been implanted with engineered grafts for dialysis access, 40 patients in Europe and 20 in the US.

The grafts can be used for dialysis access as soon as four to eight weeks after implantation. This early experience has been very positive, indicating a potential future for this novel graft in providing vascular access for hemodialysis.

Dr. Niklason's lab was one of the first to describe the engineering of whole lung tissue that could exchange gas in vivo. This work was cited in 2010 as one of the top 50 most important inventions of the year by *Time* magazine. Dr. Niklason was inducted into the National Academy of Inventors in 2014 and elected to the National Academy of Medicine in 2015.

She received her PhD in biophysics from the University of Chicago and her MD from the University of Michigan. She completed her residency in anesthesia and intensive care medicine at the Massachusetts General Hospital in Boston and her postdoctoral training at the Massachusetts Institute of Technology.

Kidney Patient Leaders to Be Recognized with the President's Medals

Paul T. Conway

Richard A. Knight, MBA

Two leaders of the American Association of Kidney Patients (AAKP) will be honored with ASN President's Medals on Thursday, Nov. 2.

Paul T. Conway is president of AAKP and Richard A. Knight, MBA, is Vice President and Chair of the Public Policy Committee for AAKP.

"Paul T. Conway and Richard Knight are tireless advocates for the millions of people with kidney diseases, their families, and their caregivers," said ASN Executive Vice President Tod Ibrahim. "This dynamic duo takes every opportunity to raise awareness about kidney diseases among the public, policymakers, politicians, and the press. In addition, they help lead the kidney community's efforts to advocate for the highest quality care possible—including increased funding for kidney research—among the legislative and regulatory branches of the U.S. government."

Mr. Conway has managed kidney disease for more than 35 years—including receiving peritoneal dialysis treatment for many years before a kidney transplant in 1997. Professionally, he has substantial experience developing and managing federal and state government policy development and legislative implementation strategies, including the engagement of stakeholder organizations and the use of social and traditional media.

Mr. Knight is a former hemodialysis patient who received a kidney transplant more than a decade ago. His professional background is in public policy and congressional operations; he has served in various roles on Capitol Hill, including as communication director, legislative director, and liaison to the Congressional Black Caucus.

Mr. Conway has experience in the private, nonprofit, and government sectors. His expertise in federal and state agency management and personnel operations was honed through service under four U.S. presidents, three governors and in support of five presidential transitions. He served as the team lead for the Office of Personnel Management on the transition team for President-elect Donald Trump.

His previous federal posts have included chief of staff of the Department of Labor, of the Office of Personnel Management, and of the Office of Gulf Coast Rebuilding within the Department of Homeland Security. He was also a special assistant in the White House Office of National Drug Control Policy.

He served the commonwealth of Virginia as a deputy secretary of health and human resources, a member of the Board of Health Professions, a member of the protection panel for homeland security planning, and an external reviewer of Virginia health, disability, and mental health modernization proposals.

As a patient advocacy leader and policy professional, Mr. Conway has used his knowledge of executive branch and congressional processes to elevate an independent patient voice on issues ranging from innovations in medical treatment and devices, improved access to treatment modalities, payment models, and quality-of-care measurements.

He serves on many national boards and committees, including the Kidney Health Initiative, the kidney committee of the United Network for Organ Sharing Kidney Committee, and the Center for Dialysis Innovation at the University of Washington. He has co-chaired several technical evaluation panels for the Centers for Medicare & Medicaid Services (CMS).

Mr. Knight also has a background in public policy and congressional affairs. While working for the U.S. House of Representatives, he was involved in substantial work with the House Energy and Commerce Committee and the Small Business Committee. He gained experience in federal agency budget and procurement policies working as a government contractor and for ten years as co-chair of the Baltimore Washington Corridor Chamber of Commerce annual regional government procurement fair.

As a small business owner, he is heavily involved in business and education issues through several executive networks in the Washington, D.C., region. He serves as adjunct professor at Bowie State University.

As a national kidney patient advocate, Mr. Knight was recently appointed to serve as a member of the National Institute of Diabetes and Digestive and Kidney Diseases advisory council and serves as an AAKP representative to a National Quality Forum working group. He has served as a member of four technical expert panels for CMS. He is a founding member of the End Stage Renal Disease Health Information Technology Project of the National Renal Administrators Association and serves on the National Kidney Disease Education Program's Health Information Technology Working Group.

Plenary Session

State-of-the-Art Lecture

Nobel Prize Winner to Speak on G-Protein-Coupled Receptors

Brian K. Kobilka, MD

A scientist who won a Nobel Prize for his work on the topic will present a state-of-the-art lecture entitled "G Protein-Coupled Receptors: Challenges for Drug Discovery" on Friday, Nov. 3.

The speaker will be Brian K. Kobilka, MD, professor of molecular and cellular physiology and Hélène Irwin Fagan Chair in Cardiology at Stanford University School of Medicine.

Research in Dr. Kobilka's lab focuses on the structure and mechanism of action of G-protein-coupled receptors (GPCRs), which constitute the largest family of receptors for hormones and neurotransmitters in the human genome. Kobilka was awarded the 2012 Nobel Prize in chemistry for this work.

GPCRs mediate the majority of cellular responses to hormones and neurotransmitters, and are therefore essential for communication between cells located in different parts of the body. GPCRs also mediate the senses of sight, smell, and some tastes. Given their role in the regulation of all aspects of human physiology, GPCRs are the targets of nearly half of today's pharmaceuticals for a broad spectrum of diseases.

GPCRs are located on the plasma membrane of cells and respond to a wide range of ligands ranging from ions to small organic molecules to peptides to large-protein hormones. GPCRs also interact with several signaling and regulatory proteins within the cell, including G proteins, kinases, and arrestins.

Dr. Kobilka's lab has used a variety of approaches to characterize the structure and mechanisms of activation of GPCRs, including cell biology, gene disruption in mice, and in vivo physiology to determine the role of specific adrenergic receptor subtypes in normal physiology.

Dr. Kobilka has served as a member of the grant-in-aid committee of the American Heart Association, a member of the molecular and integrative signal transduction study section of the National Institutes of Health, and chair of the Gordon Research Conference on Molecular Pharmacology.

He serves on the editorial boards of *Molecular Pharmacology and Trends in Pharmacological Sciences* and has been on the board of the *Journal of Biological Chemistry* as well as associate editor of *Molecular Pharmacology*.

He is a member of the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences.

Dr. Kobilka graduated from Yale University School of Medicine and completed residency training in internal medicine at the Barnes Hospital, Washington University School of Medicine in St. Louis. He was a postdoctoral fellow at Duke University from 1984 to1989. He joined the faculty of Stanford in 1990.

Researcher to Receive Homer W. Smith Award

Martin R. Pollak, MD

"Acclaimed researcher Martin R. Pollak, MD, will be presented the Homer W. Smith Award, which recognizes outstanding contributions to understanding how kidneys function in normal and diseased states, on Friday, Nov. 3.

Dr. Pollak will speak on "Kidney Disease Genetics: From Rare to Common Variants." He is professor of medicine at Harvard Medical School and chief of the division of nephrology at the Beth Israel Deaconess Medical Center.

His research has focused on the genetic basis of kidney disease, with a particular interest in identifying and understanding the genes involved in the development of focal segmental glomerulosclerosis (FSGS) in humans. Intrigued by the high rate of FSGS and hypertension-associated kidney disease in African Americans, he and his collaborators recently showed that common coding sequence variants in the APOL1 gene explain much of the high rate of kidney disease in people of recent African ancestry.

A second major focus of his study has been the extracellular calcium receptor. Dr. Pollak cloned the human calcium-sensing receptor gene and demonstrated that defects in this receptor cause three distinct disorders of extracellular calcium homeostasis.

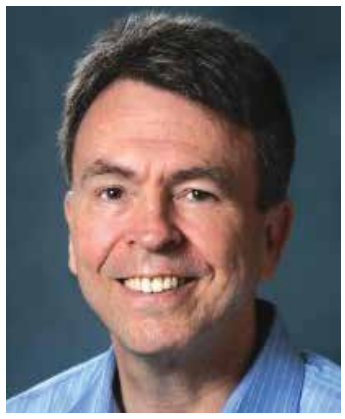
An active member of ASN, he has served on the genetics subcommittee, program committee, and basic science committee. For the National Institutes of Health (NIH), he has served on an FSGS task force and advisory committees on CRISPR gene editing technology.

Dr. Pollak has served as a consulting editor for the *Journal of Clinical Investigation* and is on the editorial boards of the *Journal of the American Society of Nephrology* and *Kidney International*.

He has been recognized with the Marilyn Farquhar Award for Podocyte Biology by the NephCure Foundation and physician scientist awards from NIH. In addition to his research and clinical activities, Dr. Pollak teaches medical students, residents, and fellows.

A graduate of the New York University School of Medicine, Dr. Pollak completed an internal medicine residency at Columbia-Presbyterian Medical Center and a nephrology fellowship at Brigham and Women's Hospital and the department of genetics at Harvard Medical School.

Patient Advocate to Examine Engagement Strategies



Kevin J. Fowler

"Effective Patient Engagement Strategies to Develop Future Therapies and Advance Patient Safety" is the title of the Celeste Castillo Lee Memorial Lectureship, scheduled for Friday, Nov. 3.

The speaker will be Kevin J. Fowler, a health care executive with more than 30 years of experience in pharmaceutical organizations.

Fowler spent more than 20 years at Pfizer, where his final position was senior director of public affairs. During a career involving a wide range of skills and experiences, he has demonstrated leadership in sales management, training, public affairs, global marketing, patient advocacy, and patient marketing.

His experience of having a preemptive kidney transplant in 2004 gave him a deep passion for patient advocacy and patient engagement. In 2014, he formed his own patient advocacy and patient engagement consulting business, The Voice of the Patient, Inc.

Fowler has brought this voice to several organizations as a volunteer, serving on the Kidney Health Initiative Patient Family Partnership Council, the advocacy committee of the National Kidney Foundation, the patient advisory group of the American Society of Transplantation, the board of directors of the American Association of Kidney Patients, and a patient advisory committee of the Kidney Research Institute.

He has designed digital patient customer relationship marketing programs and coordinated care strategies aimed at improving patient outcomes, creating brand loyalty, and reducing health care costs.

From 2007 to 2012, he served as the senior product manager for patient education and advocate relations at Astellas U.S., the U.S. affiliate of Tokyo-based Astellas Pharma. From 2013 to 2014, he served as a senior product manager for global marketing at AbbVie Inc., a biopharmaceutical company based in North Chicago, Ill.

Inflammation and Fibrosis Could Be Keys to Progression of AKI Toward CKD

Manjeri A. Venkatachalam, MBBS

The role of inflammation and fibrosis in the progression of AKI to CKD will be the subject of the Barry M. Brenner, MD, Endowed Lectureship on Friday, Nov. 3.

The speaker will be a scientist who has done extensive research on the topic, Manjeri A. Venkatachalam, MBBS, a professor in the departments of pathology, medicine, and biochemistry at the University of Texas Health Science Center in San Antonio.

Dr. Venkatachalam has a background in both clinical and basic science. He was a house physician in internal medicine for two years prior to five years training in anatomic pathology. He then gained experience as a staff physician practicing diagnostic pathology and renal pathology while conducting basic research.

His research into kidney physiology and pathology has examined proteinuria, glomerulosclerosis, and tubulointerstitial disease. Clinical and epidemiological studies point to the importance of AKI as a harbinger leading to CKD. During the past six years, his research has focused on the pathogenesis of tubulointerstitial pathology in the transition from AKI to CKD. As an early investigator of hemodynamic mechanisms that drive progression of CKD, Dr. Venkatachalam has noted the role that new AKI episodes could play by reducing available renal mass and interacting with CKD pathophysiology to compromise tubule recovery and worsen clinical status.

Dr. Venkatachalam's laboratory has worked to identify the cellular, biochemical, and signaling basis for defective tubule repair after AKI as well as the role played by failed tubule recovery in the AKI-CKD transition. His most recent research has focused on the role of nuclear and mitochondrial DNA damage in the pathogenesis of tubule atrophy after AKI and the large-scale loss of mitochondria that takes place in the dedifferentiated tubules that become atrophic.

Dr. Venkatachalam serves on the editorial boards of the *Journal of the American Society of Nephrology* and *Kidney International* and has been on the boards of *Laboratory Investigation* and the *American Journal of Pathology*.

He has served on several National Institutes of Health committees and study sections. For ASN, he has served on the program committee several times and on the acute renal failure advisory group.

He received his medical degree from the Calcutta Medical College and Calcutta University in India, with residencies at Upstate Medical Center in Syracuse, New York, and Boston City Hospital in Massachusetts.

Regulation of Sodium Transporters Will Be Lecture Subject

Alicia M. McDonough, PhD

Alicia M. McDonough, PhD, will discuss "Inflammatory Cytokines Regulate Proximal and Distal Sodium Transporters" in the Robert W. Schrier, MD, Endowed Lectureship on Friday, Nov. 3.

Dr. McDonough is professor of integrative anatomical sciences at the Keck School of Medicine of the University of Southern California (USC) in Los Angeles. Upon joining the USC faculty in 1981, she began studying the assembly of sodium pump subunits and defining the molecular mechanisms of sodium pump isoform regulation in cardiac and skeletal muscle by potassium and hormones. The McDonough lab initiated studies to determine the renal mechanisms responsible for regulation of sodium, potassium, and blood pressure balance as well as how homeostasis is disrupted in disease states and can be corrected therapeutically.

The lab recently investigated ion transporters' phosphorylation, abundance, subcellular distribution, and activity. The researchers' findings have enabled them to define how stimuli such as dietary sodium and potassium, angiotensin II, cytokines, and injury increase renal sodium transport, as well as how the resultant hypertension decreases sodium reabsorption via pressure natriuresis. To pursue these projects, the McDonough lab has engaged with collaborators across the United States. and around the world.

Dr. McDonough has published extensively and given many lectures on these topics. She has received the Established Investigator Award from the American Heart Association (AHA), the E.H. Starling Distinguished Lectureship from the American Physiological Society (APS), the Donald Seldin Lectureship from the AHA Council on the Kidney in Cardiovascular Disease, and several teaching awards.

She serves on several editorial boards, study sections, and committees for the ASN, APS, and AHA.

Dr. McDonough earned her doctorate in physiology at the University of Hawaii and was a postdoctoral scholar at the University of California, San Francisco, Cardiovascular Research Institute and Columbia University.

ASN Foundation for Kidney Research

Time for a Cure

Mission: To prevent and cure kidney diseases through research and innovation.

Established in 2012, the ASN Foundation for Kidney Research funds the ASN Pre-Doctoral Fellowship Award Program, the Ben J. Lipps Research Fellowship Program, the Career Development Grants Program, the William and Sandra Bennett Clinical Scholars Program, and the American Society of Nephrology-Harold Amos Medical Faculty Development Program Award, providing more than $3,000,000 annually to young investigators, fellows, and nephrology educators.

Founders Circle Members

Thanks to the generosity of our Founding Members, the ASN Foundation for Kidney Research endowed the Ben J. Lipps Research Fellowship Program in 2015, ensuring it continues in perpetuity. The ASN Foundation is proud to welcome Keryx Biopharmaceuticals, Inc. into the Founders Circle and to recognize the ASN Members who provided generous contributions to the Career Development Grants Program and the *Securing the Future Campaign*.

Career Development Grants Program

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Polycystic Kidney Disease

$500,000

It is the generosity of individuals and companies within the kidney community that makes change possible. With the help of our Founding Members, the ASN Foundation is making great strides in supporting the next generation of nephrology clinicians, researchers, and educators who will fuel innovation and translate findings into improved quality of life for patients.

The ASN Foundation for Kidney Research congratulates the talented group of researchers and educators who were awarded grants in 2017.

Career Development Grants Program

Funding up to nine new applicants and nine continuing projects annually, the program invests $100,000 a year per investigator for two years to foster independent research careers and ensure a pipeline of innovative research in the field of nephrology.

Carl W. Gottschalk Research Scholar Grants

Amandeep Bajwa, PhD
University of Virginia
Mitochondria Transfers to Prevent Ischemic Reperfusion Injury in Transplant

Wei Chen, MD, MS*
University of Rochester
Calcification Propensity, Using Dynamic Light Scattering, to Study Vascular Calcification in Patients with Advanced CKD

Paul G. Decaen, PhD
Northwestern University
Defining ADPKD-2 Mutation Effects on Ciliary PKD2 Ion Channels

Kevin F. Erickson, MD, MS
Baylor College of Medicine
Dialysis Facility Closures and Their Effect on Costs, Health Outcomes, and Access to Care

Aaron J. Polichnowski, PhD
East Tennessee State University
Deleterious Effects of TNF-a on the AKI-CKD Nexus

John Merrill Grant in Transplantation

Ulf H. Beier, MD
Children's Hospital of Philadelphia
NAD Redox Metabolism Controls T Cell Function

Oxalosis & Hyperoxaluria Foundation-ASN Foundation for Kidney Research Career Development Grant

Lama Nazzal, MD, MS*
New York University
Oxalate Metabolism in a Humanized Mouse Model

Norman Siegel Research Scholar Grant

John David Spencer, MD
Nationwide Children's Hospital
Insulin Signaling, Antimicrobial Peptide Production, and the Intercalated Cell's Antibacterial Defenses

The ASN Foundation for Kidney Research proudly announces a new Career Development Grant in 2018:

Joseph V. Bonventre Career Development Grant

- Funded every other year by Keryx Biopharmaceuticals, Inc. and ASN

Ben J. Lipps Research Fellowship Program

Funding ten new research applicants and ten continuing projects annually, the program distributes $50,000 a year per fellow for two years to conduct original, meritorious research.

Ben J. Lipps Research Fellows

Khodor Abou Daya, MD
University of Pittsburgh
Tissue Resident Memory T Cells in Organ Transplantation

Calyani Ganesan, MD
Stanford University
Bone Outcomes in Urinary Stone Disease: Data from the Veterans Health Administration

Ragnar Palsson, MD
Brigham and Women's Hospital
Use of Endogenous Serum Filtration Markers for Estimation of Renal Functional Reserve

Vishnu S. Potluri, MD, MPH
University of Pennsylvania
Impact of Neighborhood Environment on Phosphate Control Among Patients on Dialysis

Viktor N. Tomilin, PhD
University of Texas Health Science Center at Houston
TRPC3-Dependent Ca2+ Signaling in Collecting Duct Water Reabsorption and Osmosensitivity

Dimitrios G. Oreopoulos Research Fellow

Nikolaos Skartsis, MD, PhD
University of California, San Francisco
The Role of Granzyme B and Serine Protease Inhibitor 6 in the Homeostasis of Adoptively Transferred Regulatory T Cells in Transplantation

Donald E. Wesson Research Fellow

Claire Gerber, PhD, MPH
Northwestern University
Effects of SGLT2 Inhibition on Mineral Metabolism and Skeletal System

George B. Rathmann Research Fellow

Charles Ginsberg, MD
University of California, San Diego
The Effects of Phosphate on Microvascular Function

Jared J. Grantham Research Fellow

Matthew Lanktree, MD, PhD
McMaster University
Improving Polycystic Kidney Disease Prognostication Using Imaging, Next Generation Sequencing, and Urinary Biomarkers

Sharon Anderson Research Fellow

Jamie Lin, MD
University of Texas MD Anderson Cancer Center
The Functional Role of ARF6-GEFs in Nephrin-Mediated Podocyte Cytoskeletal Remodeling and Endocytic Nephrin Trafficking

William and Sandra Bennett Clinical Scholars Program

Funded annually, the program provides $50,000 a year for two years to a nephrology educator to conduct a project to advance all facets of nephrology education and teaching.

John K. Roberts, MD
Duke University
Pencast Videos to Boost Learning and Interest in Nephrology Among Internal Medicine Residents

**** Kidney Week 2017 oral and/or poster abstract presenter***

Plenary Session

State-of-the-Art Lecture

Epigenetics Expert to Examine Environment's Link to Disease

Andrew P. Feinberg, MD, MPH

Andrew P. Feinberg, MD, MPH, will deliver a state-of-the-art lecture entitled "Epigenetics at the Crossroad of Genetics and Environment Leading to Disease" on Saturday, Nov. 4.

Dr. Feinberg is director of the Center for Epigenetics at the Johns Hopkins University. He also holds an adjunct professorship at the Karolinska Institute in Sweden and is a presidential scholar at Harvard's Dana Farber Cancer Institute.

Dr. Feinberg made the first discoveries of altered DNA methylation in human cancer. He discovered human imprinted genes and loss of imprinting in cancer, and proved the epigenetic hypothesis of cancer through his work on Beckwith-Wiedemann syndrome. He also identified the first common genetic or epigenetic variant for cancer risk—loss of imprinting of insulin-like growth factor 2 in colorectal cancer. His discovery of epigenetically altered progenitor cells led to a paradigm shift in our understanding of carcinogenesis.

Recently, he pioneered genome-scale epigenetics with the first epigenome center funded by the National Institutes of Health (NIH). The center has pioneered methods such as the first comprehensive genome-scale methylation, which led it to identify the major target for epigenetic variation in humans. Dr. Feinberg led the first whole genome bisulfite sequencing analysis of human cancer.

He received the NIH Pioneer Award for his idea in 2009 that genetic variants, in evolution or in cancer, could lead to increased epigenetic plasticity, enhancing survival in a changing environment. His studies of metastasis driven by stochastic epigenetic change rather than metastasis-specific mutations provided evidence for this idea.

His honors include a MERIT Award from the National Cancer Institute, election to the National Academy of Medicine, and the Feodor Lynen Medal from the German Society for Biochemistry and Molecular Biology. The Institute for Scientific Information ranks him among the most cited authors.

Dr. Feinberg received his MD and MPH from Johns Hopkins University. As a postdoctoral fellow at the University of California, San Diego, he identified epigenetic memory of cell fate in *Dictyostelium*. He received clinical training in medicine at the University of Pennsylvania and in medical genetics at Johns Hopkins. As a fellow there from 1983 to 1986, he developed the random priming method, which is ranked in the top 100 papers of all time in citations. He was a Howard Hughes investigator at the University of Michigan from 1986 to 1994, and returned to Johns Hopkins as the King Fahd Professor of Medicine, Molecular Biology, and Genetics.

ASN to Bestow Belding H. Scribner Award on Raymond M. Hakim

Raymond M. Hakim, MD, PhD

The Belding H. Scribner Award will be tendered to Raymond M. Hakim, MD, PhD, on Saturday, Nov. 4, for his career-long contributions to the practice of nephrology. Dr. Hakim is professor of medicine in the division of nephrology and hypertension at the Vanderbilt University Medical Center. Established in 1995, the Belding H. Scribner Award is presented to individuals who have made outstanding contributions to the care of patients with renal disorders or have substantially influenced the clinical practice of nephrology.

Dr. Hakim has made significant contributions in patient care, research, and service to professional organizations. Dr. Hakim began his career as an engineer. He received a master of science degree from Rensselaer Polytechnic Institute and a PhD in engineering from the Massachusetts Institute of Technology in 1967. He worked in Montreal as a research engineer at Hydro-Quebec. He changed his career path to study medicine at McGill University and completed his residency in internal medicine at the Royal Victoria Hospital in 1979. He followed this with a fellowship in nephrology at Harvard Medical School and Brigham and Women's Hospital.

From 1981 to 1987, he was associate professor of medicine at Harvard and attending nephrologist at Brigham and Women's Hospital. In 1987, he became professor of medicine at Vanderbilt University School of Medicine, and medical director of the Vanderbilt University Medical Center dialysis facility.

In 1995, Dr. Hakim was one of the founders and chief medical officer of the Renal Care Group, a provider of outpatient dialysis services. By 2005, the Renal Care Group had more than 35,000 patients and had the lowest mortality and hospitalization rates among all dialysis providers, according to the United States Renal Data System (USRDS). The group merged with Fresenius Medical Care in 2007, and Dr. Hakim became the chief medical officer, serving from 2009 to 2012. His tenure was associated with a 20% reduction in mortality and hospitalization of its patients.

Dr. Hakim has spoken at many patient and health care professional meetings, authored more than 190 articles on clinical and basic research in dialysis and plasmapheresis, and contributed 35 chapters to medical books.

He has served as a member of the editorial boards of several journals and received the National Kidney Foundation Joel D. Kopple Award and the Medal of Excellence Award from the American Association of Kidney Patients.

John P. Peters Award to Honor Ronald J. Falk

Ronald J. Falk, MD, FASN

ASN will recognize the wide-ranging contributions of Ronald J. Falk, MD, FASN, with the presentation of the John P. Peters Award on Saturday, Nov. 4.

The John P. Peters Award is given for outstanding contributions to improving the lives of patients and to furthering the understanding of the kidney in health and disease.

Dr. Falk is an internationally recognized physician-scientist who has devoted more than three decades to the study of autoimmune kidney disease and ANCA vasculitis in an effort to improve the lives of patients afflicted with these conditions. His research has led to a deeper understanding of the causes and conditions that lead to the development of ANCA vasculitis.

Dr. Falk chairs the department of medicine at the University of North Carolina. He is also chair of Carolina Dialysis, LLC, and chair and co-founder of the Carolina Vascular Access Center. In 2005, he founded and became director of the UNC Kidney Center.

Dr. Falk served as ASN president from 2011 to 2012. He has served ASN in various other capacities, including on the council, finance committee, education committee, and annual meeting program committee. He has served as chair or a member of several National Institutes of Health study sections and steering committees. He founded Kidney Health Initiative, a public-private partnership with the ASN and the U.S. Food and Drug Administration.

He has served on many editorial boards, including for *Kidney International, Journal of the American Society of Nephrology, Journal of Nephrology, American Journal of Kidney Diseases*, and *American Family Physician*. His research has resulted in more than 230 publications in peer-reviewed journals, and he has contributed some 140 book chapters and reviews and more than 300 abstracts.

Dr. Falk has received a number of distinguished professorships at UNC and was most recently honored with the Nan and Hugh Cullman Eminent Professorship in 2016. He has received numerous other honors and awards, including recognition as one of the "Best Doctors in America" every year since 1982.

Dr. Falk obtained his MD from the University of North Carolina School of Medicine. He served as chief of the division of nephrology and hypertension at the University of North Carolina from 1993 through 2015.

Joel M. Topf to Be Given Robert G. Narins Award for Contributions in Education

Joel M. Topf, MD

Joel M. Topf, MD, will receive the Robert G. Narins Award on Saturday, Nov. 4, for his innovative efforts to incorporate the latest forms of electronic communication and social media into medical education. Dr. Topf is partner at St. Clair Nephrology and an assistant clinical professor at Oakland University William Beaumont School of Medicine in the Detroit metro area.

He became involved in medical education before he even graduated from medical school. During his third year at Wayne State University medical school, he and fellow student Sarah Faubel wrote a microbiology study guide for medical students that they sold nationwide. This unexpected success inspired a second endeavor. During his internal medicine and pediatrics residency at Indiana University, he wrote a book about nephrology entitled, *The Fluid, Electrolyte, and Acid-Base Companion*.

After his nephrology fellowship residency at the University of Chicago, Dr. Topf returned to Detroit and began working at St. Clair Nephrology. In addition to his hospital rounds, clinic time, and dialysis duties, he continued to teach. In 2008, he started one of the first nephrology blogs, Precious Bodily Fluids, named after the obsession he shared with one of the characters in Stanley Kubrick's Dr. Strangelove.

As the number of nephrologists interested in online education grew, in 2011 he joined with Kenar D. Jhaveri, MD, FASN, and Matthew A. Sparks, MD, FASN, to establish the official blog of the *American Journal of Kidney Diseases*. This landmark event turned blogging and social media medical education from a solo to a collaborative practice.

In 2013, Dr. Sparks and Dr. Topf created NephMadness, an online educational game that leverages the excitement surrounding the U.S. collegiate basketball tournament known as March Madness. NephMadness continues to be a high-profile, social media-based, educational campaign with participants from around the world. It involves dozens of people working to generate educational content.

The next year, Dr. Topf joined with Swapnil Hiremath to create NephJC, a journal club that uses Twitter to discuss the research, guidelines, and editorials that are driving nephrology. The outlet has reviewed more than 70 articles and engages 150 nephrologists with each discussion.

Dr. Topf is currently working with other early adopters to teach social media skills to the next generation of nephrologists through the Nephrology Social Media Collective Internship. He is helping the *Clinical Journal of the American Society of Nephrology* to incorporate the new medium of visual abstracts. He serves on the ASN Communications and Media Committee.

He is also an assistant clinical professor at the Wayne State University School of Medicine and the Oakland University William Beaumont School of Medicine.

Talk Will Focus on Genetic Factors in Kidney Diseases

Jeffrey B. Kopp, MD

A researcher with decades of experience will examine genetic factors in kidney diseases in the Michelle P. Winn, MD, Endowed Lectureship on Saturday, Nov. 4. Jeffrey B. Kopp, MD, will speak on "APOL1 Risk Alleles and the Podocyte."

Dr. Kopp is chief of the kidney diseases branch at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in Bethesda, Md. He serves as a consultant on the nephrology service at the National Institutes of Health (NIH) Clinical Center.

Dr. Kopp leads a translational research group studying FSGS and related podocyte diseases. His group's genetic studies contributed to the identification of APOL1 as a major susceptibility gene for kidney diseases in African Americans. He will describe some of the recent highlights of their work, including the discovery that chromosome 22 harbors a major risk locus for kidney diseases in African Americans, including FSGS, HIV-associated nephropathy, and arterionephrosclerosis (hypertension-attributed kidney disease). APOL1 coding variants, which protect against trypanosomal infection, are strongly associated with kidney diseases. Dr. Kopp is continuing this research to try to identify the mechanisms by which APOL1 variants damage the glomerulus. He has published over 290 scientific papers.

He has served on several editorial boards, including those of the *American Journal of Kidney Disease, American Journal of Nephrology, American Journal of Physiology*, and *Kidney International*. He was the issue editor of an edition of *Seminars in Nephrology* that focused on FSGS.

He has served on the organizing committee for several NIDDK conferences and been on the ASN program committee.

Dr. Kopp began his career at NIH as a medical staff fellow in 1987 and became a senior investigator in 1995. He also serves as an adjunct professor of medicine in the Uniformed Services University of the Health Sciences.

He holds a commission with the rank of captain in the U.S. Public Health Service and participates in the rapid deployment force to provide a medical response to natural disasters. He attended the University of Pennsylvania Medical School and trained in internal medicine and nephrology at the University of Washington.

Coburn Lecture Will Cover Mineral Metabolism in CKD

Tamara Isakova, MD, MMSc

A pioneer in researching mineral metabolism will deliver the Jack W. Coburn, MD, Endowed Lectureship, entitled "Longitudinal Studies of Mineral Metabolism in CKD," on Saturday, Nov. 4.

The speaker will be Tamara Isakova, MD, MMSc, who is associate professor of medicine in the division of nephrology and hypertension as well as director of the Center for Translational Metabolism at the Northwestern University Feinberg School of Medicine.

Dr. Isakova has an active clinical practice, providing care for patients with CKD, kidney stones, and bone and mineral metabolism disorders. She conducts clinical research on disorders of mineral metabolism in CKD. She has published more than 70 original investigations, reviews, and book chapters; her research has been supported by the American Kidney Fund, the American Heart Association, the American Society of Nephrology (ASN), and the National Institutes of Health.

She has received many awards, including a junior faculty award from the University of Miami Miller School of Medicine and the Carl W. Gottschalk Research Scholar Award from ASN.

She is a member of the editorial board of the *Clinical Journal of the American Society of Nephrology* and a reviewer for 17 journals.

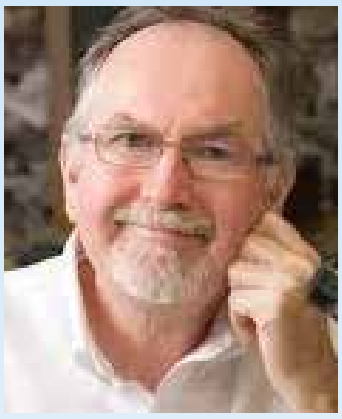
Among her many professional activities, she was abstract category chair for the 2014 ASN annual meeting, a program committee member for the 2015 ASN Kidney Week, a member of the clinical scientist in nephrology committee of the American Kidney Fund, and a member of the National Kidney Foundation expert panel on the role of vitamin D in stage 3–4 CKD.

A graduate of the State University of New York Downstate College of Medicine, Dr. Isakova completed internal medicine training at Massachusetts General Hospital and nephrology training in the combined fellowship program of Massachusetts General Hospital and Brigham & Women's Hospital.

Plenary Session

State-of-the-Art Lecture

Role of Immunity in Tissue Injury to Be Lecture Topic



Richard A. Flavell, PhD, DSc

A state-of-the-art lecture will cover the topic "Innate Immunity in Tissue Injury and Inflammation" on Sunday, Nov. 5.

Richard A. Flavell, PhD, DSc, will deliver the talk. He is Sterling Professor of Immunobiology at Yale University School of Medicine and an investigator at the Howard Hughes Medical Institute.

Dr. Flavell is co-discoverer of introns in cellular genes. He showed that DNA methylation correlates inversely with, and prevents, gene expression. He was the first to develop reverse genetics and has become a sophisticated practitioner in the use of this approach in vivo to study function.

Dr. Flavell's laboratory studies the molecular and cellular basis of the immune response, particularly as it applies to autoimmune and autoinflammatory diseases. The researchers have discovered the role of several receptor families in the innate immune response, including the role of several Toll-like receptors and intracellular Nod-like receptor families. These discoveries have led to the elucidation of the function of Nod2 in inflammatory bowel diseases and NLRP proteins in the production of interleukin-1.

Dr. Flavell has been instrumental in discovering the molecular basis of T-cell differentiation from precursor cells into differentiated subsets and provided the first example of gene regulation via direct physical interactions between pairs of chromosomes, a phenomenon known as "kissing chromosomes." His laboratory has also elucidated the mechanisms of immunoregulation that prevent autoimmunity and overaggressive responses to pathogens.

Dr. Flavell has published more than 1000 peer-reviewed papers and is one of the world's most cited immunologists.

Dr. Flavell is a fellow of the Royal Society and a member of the National Academy of Sciences and the National Academy of Medicine.

Dr. Flavell served as the founding chair of Yale's department of immunobiology for 28 years, stepping down in early 2016. Prior to joining Yale in 1988, Dr. Flavell was an assistant professor at the University of Amsterdam; head of the Laboratory of Gene Structure and Expression at the National Institute for Medical Research in the UK; and president and chief scientific officer of Biogen Research Corporation in Cambridge, Mass.

He received his PhD in biochemistry from the University of Hull in England, and performed postdoctoral work at the University of Amsterdam and the University of Zurich.

Young Investigator Recognized for Leadership on AKI Biomarkers

Chirag R. Parikh, MD, PhD

The ASN-AHA Young Investigator Award and Address will be presented to Chirag R. Parikh, MD, PhD, who will speak on "Biomarkers for Phenotyping Clinical AKI: Optimizing Questions, Tools, and Trials" on Sunday, Nov. 5.

Dr. Parikh is professor of medicine and investigative medicine and director of the Program of Applied Translational Research at the Yale School of Medicine.

Recognized internationally for his accomplishments in the study of AKI and biomarkers, Dr. Parikh is leading a paradigm change by generating evidence for various clinical applications of structural injury biomarkers in AKI. He has created major multi-disciplinary consortia, developed a large biosample repository, and designed a robust mentoring program to pave the way for continued research innovation.

In 2005, Dr. Parikh established the Translational Research Investigating Biomarker End-points (TRIBE) Consortium, a multidisciplinary collaboration of 11 academic centers in North America. Funded by the National Institutes of Health (NIH), the TRIBE Consortium has conducted several prospective cohort studies for the discovery and validation of kidney biomarkers. It has enrolled more than 5000 patients to evaluate complications after cardiac surgery and collected over 500,000 blood and urine samples to evaluate the role of kidney injury markers of apoptosis, inflammation, injury, and repair. This effort enabled Dr. Parikh to perform the largest validation study to date of urinary biomarkers in kidney injury after cardiac surgery, which has resulted in the development of several biomarkers.

Dr. Parikh was also among the first to provide evidence that AKI is not simply a temporary and reversible co-morbidity, but rather a condition associated with long-term mortality and chronic kidney disease. He published the first study to demonstrate the association of longer-term mortality with kidney injury biomarkers. His findings are being translated rapidly to clinical practice by the inclusion of structural biomarkers in upcoming AKI guidelines.

In addition to his work in AKI, Dr. Parikh has initiated large, NIH-funded, multicenter studies in the areas of deceased-donor kidney transplantation, hepatorenal syndrome, HIV nephropathy, and diabetic kidney disease. Dr. Parikh has published more than 250 peer-reviewed articles.

Dr. Parikh has received consistent outstanding teacher reviews from medical students and nephrology fellows. He has attracted so many fellows and residents to his research program that his trainees are listed as the first author on more than 70 publications. In 2011, he received the prestigious NIH K24 Mid-Career Research Mentoring Award.

Dr. Parikh earned his MD from Seth G.S. Medical College in Mumbai and completed his internal medicine training at Nassau University Hospital and SUNY Stony Brook in New York. He completed his nephrology fellowship and earned his PhD in clinical investigation at the University of Colorado School of Medicine.

KIDNEYWEEK 2017

New Orleans, LA • Oct 31 - Nov 5

Educational Symposia SCHEDULE

Thursday, November 2 – Saturday, November 4

12:45–1:45 p.m. *(Doors open at 12:30 p.m.)*

Hilton New Orleans Riverside

Continuing Education Credit

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

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.

Thursday, November 2

Anemia in Kidney Diseases: Beyond the Usual Suspects*
St. Charles Ballroom
Support is provided by an educational grant from ***AstraZeneca and FibroGen.***

Hyperparathyroidism in Chronic Hemodialysis Patients: What Should I Do?
Grand Salon 1
This activity is supported by educational funding provided by ***Amgen***.

Management of Hyperkalemia in Patients on RAAS Blockade*
Grand Ballroom A
Support is provided by an educational grant from ***Relypsa, Inc***.

Onward and Upward: Hepatitis C Prevention and Treatment*
Grand Ballroom C
Support is provided by an educational grant from ***Merck***.

Friday, November 3

Basic Science Symposium: Single-Cell Sequencing to Understand Cellular Heterogeneity and Function
St. Charles Ballroom
Sponsored by the ***American Society of Nephrology (ASN)***.

Cystine: One Amino Acid – Two Renal Outcomes*
Grand Salon 1
Support is provided by an educational grant from ***Horizon Pharma USA, Inc.***

Hypoxia-Inducible Factor Stabilizers: A Physiologic Approach to Treat Anemia of CKD*
Grand Ballroom C
Support is provided by an educational grant from ***Akebia Therapeutics, Inc***.

Phosphorus Management in CKD and ESRD: A Long Road to Travel
Grand Ballroom A
Support is provided by an educational grant from ***Fresenius Medical Care Renal Therapies Group***.

Saturday, November 4

ADPKD: Advances in Pathogenesis and Treatment*
Grand Ballroom C
Support is provided by an educational grant from ***Otsuka America Pharmaceutical, Inc***.

Fluid Management and Patient Outcomes in Hemodialysis: Goal Weight or Ultrafiltration Rate?*
Grand Ballroom A
Support is provided by an educational grant from ***Fresenius Medical Care Renal Therapies Group***.

Going (Anti) Viral: New Approaches for Treating Hepatitis C*
St. Charles Ballroom
Support is provided by an educational grant from ***AbbVie***.

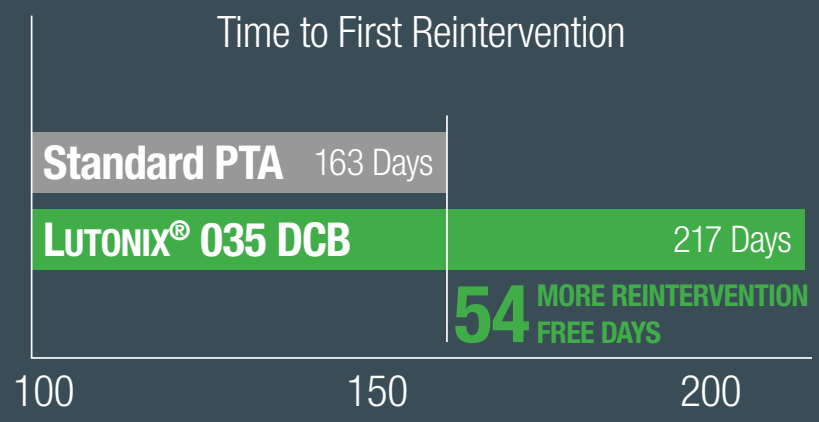
How Should I Administer Iron for the Management of Anemia in CKD?*
Grand Salon 1
Support is provided by an educational grant from ***Keryx Biopharmaceuticals, Inc***.

**Session will be recorded and available online in the ASN Learning Center in January. Continuing education credits will not be awarded for this content.*

ASN

Reduced Reinterventions for Dysfunctional AV Fistulae

The LUTONIX® 035 Drug Coated Balloon PTA Catheter enabled **longer AV fistulae function** due to **fewer reinterventions** compared to standard angioplasty. LUTONIX® 035 DCB demonstrated **71.4% Primary Patency** at 6 months versus PTA.



4-12 mm
Diameters Available

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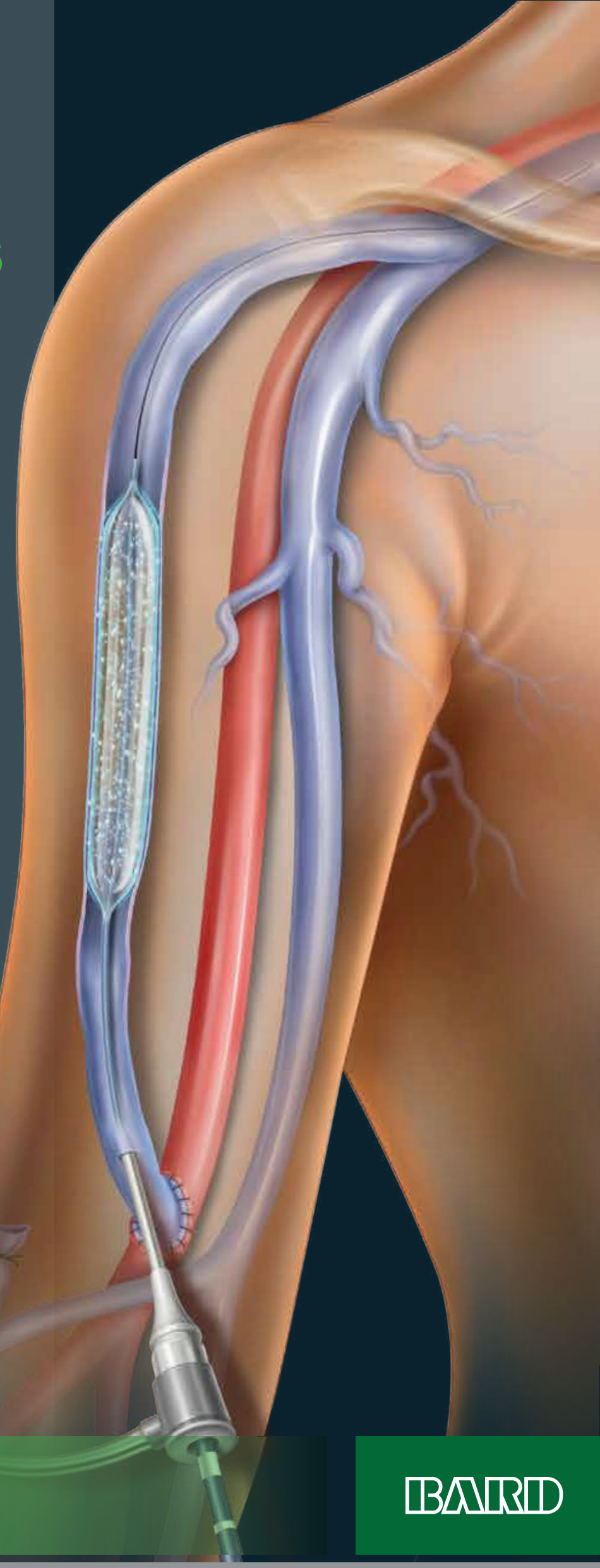
Fewer Reinterventions
than PTA at 6 Months



LUTONIX® 035
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LUTONIX® AV Clinical Trial data on file. N=285. At 6 months, treatment with LUTONIX® 035 DCB resulted in a primary patency rate of 71.4% versus 63.0% with PTA alone. Primary patency defined as ending with a clinically driven re-intervention of the target lesion or access thrombosis. The primary effectiveness analysis for superiority of DCB vs. PTA was not met with a one sided p-value of p = 0.0562. Number of interventions required to maintain TLP at 6 months were 44 in DCB arm versus 64 in the PTA arm. At 30 days, treatment with LUTONIX® 035 resulted in a freedom from primary safety event rate of 95.0% versus 95.8% with PTA alone. Primary safety defined as freedom from localized or systemic serious adverse events through 30 days that reasonably suggests the involvement of the AV access circuit. The primary safety endpoint for non-inferiority for DCB vs. PTA was met with one-sided p-value of p = 0.0019. Percentages reported are derived from Kaplan-Meier analyses.
The LUTONIX® Catheter is indicated for percutaneous transluminal angioplasty (PTA), after pre-dilatation, for treatment of stenotic lesions of dysfunctional native arteriovenous dialysis fistulae that are 4 mm to 12 mm in diameter and up to 80 mm in length.
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Serum suPAR Said to Predict Pediatric Kidney Disease Progression

By Bridget M. Kuehn

Higher serum soluble urokinase receptor (suPAR) levels are associated with a higher risk of CKD progression in children, according to a study in *JAMA Pediatrics*.

The findings are the latest to suggest suPAR may be a useful biomarker for predicting onset or progression of kidney disease. A 2015 study in the *New England Journal of Medicine* showed that elevated levels of suPAR are linked with the incidence of CKD and faster decline of renal function in adult patients (Hayek SS, et al. *N Engl J Med* 2015; 373:1916–1925).

Not having good early biomarkers can hamper treatment for kidney disease.

"Time after time, research has shown that treatments need to be given early in the course of the disease to be the most effective," said Michael Bennett, PhD, assistant professor of pediatrics and director of the Biomarker Laboratory at Cinncinati Children's Hospital Medical Center. "Finding earlier markers of kidney disease and its progression can allow physicians to make better informed decisions as to the course of treatment for the patients. Earlier implementation of those treatments may lead to better outcomes."

Nephrologists rely on biomarkers like creatinine, estimated glomerular filtration rate (eGFR), and protein in urine to identify adults and children with kidney disease. But these markers don't do well at predicting which individuals will progress from normal kidney function to CKD or have a faster decline during kidney disease, said pediatric nephrologist Howard Trachtman, MD, professor of pediatrics at NYU Langone Medical Center, co-author of both studies.

Especially challenging is predicting kidney disease in children whose kidney dysfunction may stem from congenital disorders or diverse etiologies, Trachtman said. Two-thirds of children in the study had congenital malformations of the renal or urogenital tract, noted co-author Jochen Reiser, professor and chair of the Department of Internal Medicine at Rush University Medical Center in Chicago. Kidney disease in adults is most often caused by diabetes, hypertension, and polycystic kidney disease, Reiser noted.

"It's a vastly different population [than adult kidney disease patients]," said Reiser.

Trachtman, Reiser, and colleagues performed a post-hoc analysis of two European prospective follow-up studies of pediatric CKD: 642 children from the 4C Study and 256 from the ESCAPE trial. About 70% of children had congenital anomalies of the kidneys and urinary tract; other diagnoses included tubulointerstitial nephropathies, glomerulopathies, and postischemic CKD. More than 60% were male; mean baseline age was 11.9 years and mean eGFR 36 mL/min/1.73 m^2.

Associations between baseline suPAR and eGFR during up to 8 years of follow-up were analyzed. Disease progression was defined as 50% loss of eGFR lasting for at least 1 month, start of renal replacement therapy, and/or eGFR < 10 mL/min/1.73 m^2.

High suPAR levels were associated with worse outcomes. Rates of endpoint-free renal survival at 5 years were 64.5% for children in the lowest quartile of baseline suPAR compared to 35.9% for those in the highest quartile. Independent risk factors for the primary endpoint were diagnosis of glomerulopathy, older age, higher blood pressure, proteinuria, and lower eGFR. Among 269 children with a baseline eGFR > 40 mL/min/1.73 m^2, higher suPAR levels were associated with a fivefold increase in risk of CKD progression: adjusted hazard ratio 5.12.

"We were very surprised to see the prediction [of kidney disease progression] was as strong as in adults or stronger," Reiser said.

Despite the study's promising findings, Bennett noted a few limitations: suPAR was measured at one time point so the study can't track changes over time, and study participants had established kidney disease by traditional measures, so "it is not clear whether suPAR will be useful early in the clinical course with milder disease."

"While any additional early information that can be found to help diagnose or track progression earlier in patients is likely to lead to improved outcomes down the road, more investigation needs to be completed before this finds its way into the daily practice of nephrologists," Bennett said.

"It can take a decade or more for new biomarkers to go through enough studies to be trusted in making decisions clinically," Bennett said. "Even then single markers are not typically useful on their own to make clinical decisions; they usually need to be combined with other markers, whether traditional markers like eGFR, or other novel biomarkers, to provide the most complete clinical picture."

In the meantime, the study provides some valuable insights into the relationship between suPAR and kidney disease. For example, while much study of suPAR has focused on its role in focal segmental glomerulosclerosis (FSGS), it appears to be involved in other forms of kidney disease as well.

Also, researchers studying the molecular mechanisms of kidney disease may want to take a closer look at suPAR's role and how it interacts with other molecules known to contribute to kidney disease and whether it might be a potential target for therapies.

"It's really a novel concept that there is something outside the kidney in the blood, probably coming from the bone marrow, dominating de novo but also existing kidney disease," Reiser said.

The researchers would like to do another study in which they follow children born with congenital malformations but otherwise functioning kidneys to determine if suPAR might predict progression in this subpopulation.

Preclinical studies are also underway to better understand how suPAR might be linked with kidney decline. Already, researchers have found that suPAR binds to integrins and podocytes, but other mechanisms may be involved, Reiser said. Trachtman said he hoped this work would ultimately lay the groundwork for clinical trials of interventions based on the underlying biology.

ASN 2017 Scientific Exposition

Thursday, November 2 – Saturday, November 4

Highlights Include

- Over 160 Exhibiting Companies
- ASN Communities Lounge
- ASN Services
  - ▲ General Information, Foundation, KHI, Membership Services, NTDS Project, and Publications
- Attendee Lounges
- Career Fair
- Complimentary Refreshment Breaks
- Exhibitor Spotlights
- "Locate Me" Kiosks – Posters/Exhibitors
- Poster Sessions
- Welcome Reception
- Wi-Fi

Welcome Reception

Thursday, November 2
6:30 p.m. – 7:30 p.m.

ASN will host a Welcome Reception in the exhibit hall the evening of Thursday, November 2.

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Communities Lounge
Aisle 900

NEW AT KIDNEY WEEK, the Communities Lounge will be a focal point of your exhibit hall experience. Visit the lounge to learn more about ASN Communities online forum, meet the leaders, network with your peers and unwind at the relaxation zone.

Exhibits and Posters
Halls G – I ▪ 9:30 a.m. – 2:30 p.m.

Exhibitor Spotlight Schedule

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

Thursday, November 2	Friday, November 3	Saturday, November 4
10:00 a.m. – 11:00 a.m. Theater 1	**10:00 a.m. – 11:00 a.m. Theater 1**	**10:00 a.m. – 11:00 a.m. Theater 1**
Pioneering a Novel Approach to Relieve CKD-Associated Pruritus: Targeting Peripheral Kappa Opioid Receptors *Presented by* CARA THERAPEUTICS	Expanded Hemodialysis: Translating Innovation to Clinical Solution *Presented by* Baxter	Rituxan (Rituximab) for the Treatment of Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) *Presented by* Genentech, A Member of the Roche Group
11:00 a.m. – 12:00 p.m. Theater 2	**11:00 a.m. – 12:00 p.m. Theater 2**	**11:00 a.m. – 12:00 p.m. Theater 2**
Beyond Membrane Stabilization and Potassium Shift: Use of Patiromer in the Inpatient Setting *Presented by* relypsa, A Vifor Pharma Company	Auryxia® (ferric citrate) Clinical Review *Presented by* KERYX BIOPHARMACEUTICALS, INC	Understanding and Treating Chronic Hepatitis C Infection in Patients with Chronic Kidney Disease *Presented by* MERCK
12:00 p.m. – 1:00 p.m. Theater 1	**12:00 p.m. – 1:00 p.m. Theater 1**	**12:00 p.m. – 1:00 p.m. Theater 1**
Managing Phosphorus with Velphoro® (sucroferric oxyhydroxide) Tablets: Proven Results in Both Clinical and Real World Settings *Presented by* FRESENIUS MEDICAL CARE, RENAL THERAPIES GROUP	The Thrombotic Microangiopathies in Your Clinical Practice: A Discussion on Identifying Patients with Atypical Hemolytic Uremic Syndrome *Presented by* ALEXION®	A New Therapeutic Agent for Chronic Hepatitis C Infection in Patients with Chronic Kidney Disease *Presented by* abbvie
1:00 p.m. – 2:00 p.m. Theater 2	**1:00 p.m. – 2:00 p.m. Theater 2**	**1:00 p.m. – 2:00 p.m. Theater 2**
Managing Iron Deficiency Anemia in the Clinical Context of NDD-CKD *Presented by* Daiichi-Sankyo	Treatment of Proteinuria in Nephrotic Syndrome: An Interactive Case-based Discussion *Presented by* Mallinckrodt Pharmaceuticals	Nephrologists on the Frontline of Fabry Disease Diagnosis and Management *Presented by* SANOFI GENZYME

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Loma Linda University
Faculty Medical Group, Transplant Institute,
is seeking a Transplant Nephrologist

Loma Linda University Faculty Medical Group, Transplant Institute, is seeking a Transplant Nephrologist.

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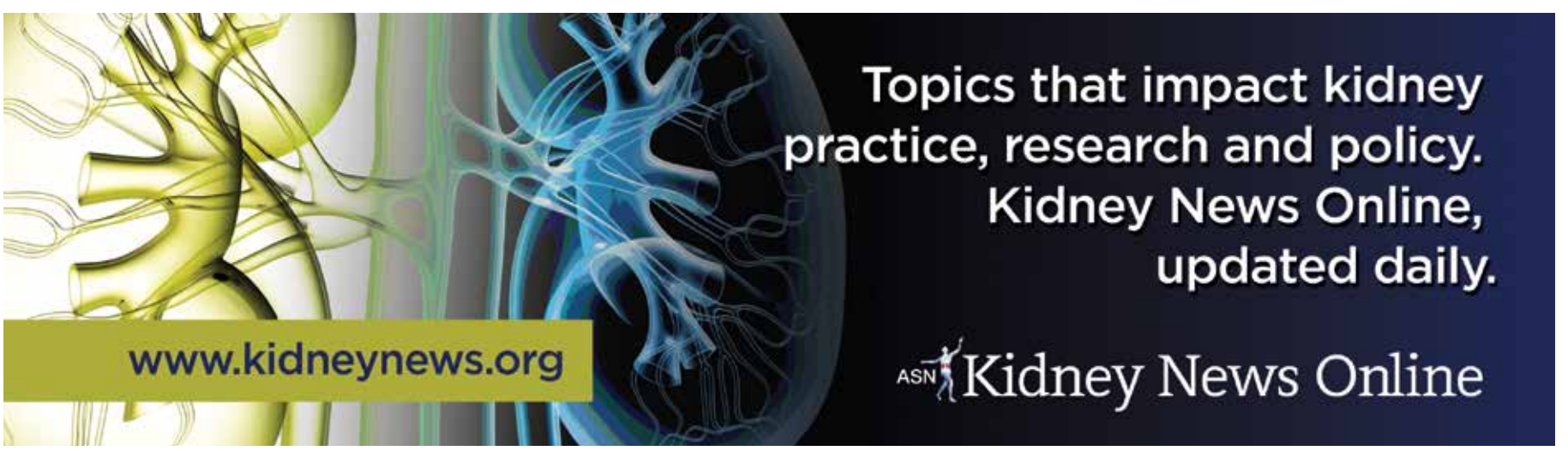


BRIEF SUMMARY OF PRESCRIBING INFORMATION

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE

PARSABIV is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

PARSABIV has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with chronic kidney disease who are not on hemodialysis and is not recommended for use in these populations.

CONTRAINDICATIONS

Hypersensitivity

PARSABIV is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred with PARSABIV *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]*.

WARNINGS AND PRECAUTIONS

Hypocalcemia

PARSABIV lowers serum calcium *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]* and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmia.

QT Interval Prolongation and Ventricular Arrhythmia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). In these studies, the incidence of a maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]*. Patients with congenital long QT syndrome, history of QT interval prolongation, family history of long QT syndrome or sudden cardiac death, and other conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to PARSABIV. Closely monitor corrected serum calcium and QT interval in patients at risk receiving PARSABIV.

Seizures

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to PARSABIV. Monitor corrected serum calcium in patients with seizure disorders receiving PARSABIV.

Concurrent administration of PARSABIV with another oral calcium-sensing receptor agonist could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to PARSABIV should discontinue cinacalcet for at least 7 days prior to initiating PARSABIV *[see Dosage and Administration (2.4) in PARSABIV full prescribing information]*. Closely monitor corrected serum calcium in patients receiving PARSABIV and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of PARSABIV. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with PARSABIV *[see Dosage and Administration (2.2) in PARSABIV full prescribing information]*. Educate patients on the symptoms of hypocalcemia, and advise them to contact a healthcare provider if they occur.

If corrected serum calcium falls below the lower limit of normal or symptoms of hypocalcemia develop, start or increase calcium supplementation (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration). PARSABIV dose reduction or discontinuation of PARSABIV may be necessary *[see Dosage and Administration (2.2) in PARSABIV full prescribing information]*.

Worsening Heart Failure

In clinical studies with PARSABIV, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. In clinical studies, heart failure requiring hospitalization occurred in 2% of PARSABIV-treated patients and 1% of placebo-treated patients. Reductions in corrected serum calcium may be associated with congestive heart failure, however, a causal relationship to PARSABIV could not be completely excluded. Closely monitor patients treated with PARSABIV for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding

In clinical studies, two patients treated with PARSABIV in 1253 patient-years of exposure had upper gastrointestinal (GI) bleeding noted at the time of death while no patient in the control groups in 384 patient-years of exposure had upper GI bleeding noted at the time of death. The exact cause of GI bleeding in these patients is unknown, and there were too few cases to determine whether these cases were related to PARSABIV.

Patients with risk factors for upper GI bleeding (such as known gastritis, esophagitis, ulcers, or severe vomiting) may be at increased risk for GI bleeding while receiving PARSABIV treatment. Monitor patients for worsening of common GI adverse reactions of nausea and vomiting associated with PARSABIV *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]* and for signs and symptoms of GI bleeding and ulcerations during PARSABIV therapy. Promptly evaluate and treat any suspected GI bleeding.

Adynamic Bone

Adynamic bone may develop if PTH levels are chronically suppressed. If PTH levels decrease below the recommended target range, the dose of vitamin D sterols and/or PARSABIV should be reduced or therapy discontinued. After discontinuation, resume therapy at a lower dose to maintain PTH levels in the target range *[see Dosage and Administration (2.1) in PARSABIV full prescribing information]*.

ADVERSE REACTIONS

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

- Hypocalcemia *[see Warnings and Precautions (5.1) in PARSABIV full prescribing information]*
- Worsening Heart Failure *[see Warnings and Precautions (5.2) in PARSABIV full prescribing information]*
- Upper Gastrointestinal Bleeding *[see Warnings and Precautions (5.3) in PARSABIV full prescribing information]*
- Adynamic Bone *[see Warnings and Precautions (5.4) in PARSABIV full prescribing information]*

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 with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The data in Table 2 are derived from two placebo-controlled clinical studies in patients with chronic kidney disease and secondary hyperparathyroidism on hemodialysis. The data reflect exposure of 503 patients to PARSABIV with a mean duration of exposure to PARSABIV of 23.6 weeks. The mean age of patients was approximately 58 years, and 60% of the patients were male. Of the total patients, 67% were Caucasian, 28% were Black or African American, 2.6% were Asian, 1.2% were Native Hawaiian or Other Pacific Islander, and 1.6% were categorized as Other.

Table 2 shows common adverse reactions associated with the use of PARSABIV in the pool of placebo-controlled studies. These adverse reactions occurred more commonly on PARSABIV than on placebo and were reported in at least 5% of patients treated with PARSABIV.

Table 2: Adverse Reactions Reported in ≥ 5% of PARSABIV-Treated Patients

Adverse Reaction*	Placebo (N = 513)	PARSABIV (N = 503)
Blood calcium decreased[a]	10%	64%
Muscle spasms	7%	12%
Diarrhea	9%	11%
Nausea	6%	11%
Vomiting	5%	9%
Headache	6%	8%
Hypocalcemia[b]	0.2%	7%
Paresthesia[c]	1%	6%

*Included adverse reactions reported with at least 1% greater incidence in the PARSABIV group compared to the placebo group

[a] Asymptomatic reductions in calcium below 7.5 mg/dL or clinically significant asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management)

[b] Symptomatic reductions in corrected serum calcium < 8.3 mg/dL

[c] Paresthesia includes preferred terms of paresthesia and hypoesthesia

Other adverse reactions associated with the use of PARSABIV but reported in < 5% of patients in the PARSABIV group in the two placebo-controlled clinical studies were:

- Hyperkalemia: 3% and 4% for placebo and PARSABIV, respectively.
- Hospitalization for Heart Failure: 1% and 2% for placebo and PARSABIV, respectively.
- Myalgia: 0.2% and 2% for placebo and PARSABIV, respectively.
- Hypophosphatemia: 0.2% and 1% for placebo and PARSABIV, respectively.

Description of Selected Adverse Reactions

Hypocalcemia

In the combined placebo-controlled studies, a higher proportion of patients on PARSABIV developed at least one corrected serum calcium value below 7.0 mg/dL (7.6% PARSABIV, 3.1% placebo), below 7.5 mg/dL (27% PARSABIV, 5.5% placebo), and below 8.3 mg/dL (79% PARSABIV, 19% placebo). In the combined placebo-controlled studies, 1% of patients in the PARSABIV group and 0% of patients in the placebo group discontinued treatment due to an adverse reaction attributed to a low corrected serum calcium.

Hypophosphatemia

In the combined placebo-controlled studies, 18% of patients treated with PARSABIV and 8.2% of patients treated with placebo had at least one measured phosphorus level below the lower normal limit (i.e., 2.2 mg/dL).

QTc Interval Prolongation Secondary to Hypocalcemia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). The patient incidence of maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively.

Hypersensitivity

In the combined placebo-controlled studies, the subject incidence of adverse reactions potentially related to hypersensitivity was 4.4% in the PARSABIV group and 3.7% in the placebo group. Hypersensitivity reactions in the PARSABIV group were pruritic rash, urticaria, and face edema.

Immunogenicity

As with all peptide therapeutics, there is potential for immunogenicity. The detection of anti-drug binding antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to etelcalcetide with the incidence of antibodies to other products may be misleading.

In clinical studies, 7.1% (71 out of 995) of patients with secondary hyperparathyroidism treated with PARSABIV for up to 6 months tested positive for binding anti-etelcalcetide antibodies. Fifty-seven out of 71 had pre-existing anti-etelcalcetide antibodies.

No evidence of altered pharmacokinetic profile, clinical response, or safety profile was associated with pre-existing or developing anti-etelcalcetide antibodies. If formation of anti-etelcalcetide binding antibodies with a clinically significant effect is suspected, contact Amgen at 1-800-77-AMGEN (1-800-772-6436) to discuss antibody testing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no available data on the use of PARSABIV in pregnant women. In animal reproduction studies, effects were seen at doses associated with maternal toxicity that included hypocalcemia. In a pre- and post-natal study in rats administered etelcalcetide during organogenesis through delivery and weaning, there was a slight increase in perinatal pup mortality, delay in parturition, and transient effects on pup growth at exposures 1.8 times the human exposure for the clinical dose of 15 mg three times per week. There was no effect on sexual maturation, neurobehavioral, or reproductive function in the rat offspring. In embryo-fetal studies, when rats and rabbits were administered etelcalcetide during organogenesis, reduced fetal growth was observed at exposures 2.7 and 7 times exposures for the clinical dose, respectively.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

There were no effects on embryo-fetal development in Sprague-Dawley rats when etelcalcetide was dosed at 0.75, 1.5, and 3 mg/kg/day by the intravenous route during organogenesis (pre-mating to gestation day 17) at exposures up to 1.8 times human exposures at the clinical dose of 15 mg three times per week based on AUC. No effects on embryo-fetal development were observed in New Zealand White rabbits at doses of etelcalcetide of 0.375, 0.75, and 1.5 mg/kg by the intravenous route (gestation day 7 to 19), representing up to 4.3 times human exposures based on AUC. In separate studies at higher doses of 4.5 mg/kg in rats (gestation days 6 to 17) and 2.25 mg/kg in rabbits (gestation days 7 to 20), representing 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

In a pre- and post-natal development study in Sprague-Dawley rats administered etelcalcetide at 0.75, 1.5, and 3 mg/kg/day by the intravenous route (gestation day 7 to lactation day 20), there was a slight increase in perinatal pup mortality, delay in parturition, and transient reductions in post-natal growth at 3 mg/kg/day (representing 1.8-fold human exposures at the clinical dose of 15 mg three times per week based on AUC), associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption. There were no effects on sexual maturation, neurobehavioral, or reproductive function at up to 3 mg/kg/day, representing exposures up to 1.8-fold human exposure based on AUC.

Lactation

Risk Summary

There are no data regarding the presence of PARSABIV in human milk or effects on the breastfed infant or on milk production. Studies in rats showed [^{14}C]-etelcalcetide was present in the milk at concentrations similar to plasma. Because of the potential for PARSABIV to cause adverse effects in breastfed infants including hypocalcemia, advise women that use of PARSABIV is not recommended while breastfeeding.

Data

Presence in milk was assessed following a single intravenous dose of [^{14}C]-etelcalcetide in lactating rats at maternal exposures similar to the exposure at the human clinical dose of 15 mg three times per week. [^{14}C]-etelcalcetide-derived radioactivity was present in milk at levels similar to plasma.

Pediatric Use

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

Geriatric Use

Of the 503 patients in placebo-controlled studies who received PARSABIV, 177 patients (35.2%) were ≥ 65 years old and 72 patients (14%) were ≥ 75 years old.

No clinically significant differences in safety or efficacy were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old). No differences in plasma concentrations of etelcalcetide were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old).

OVERDOSAGE

There is no clinical experience with PARSABIV overdosage. Overdosage of PARSABIV may lead to hypocalcemia with or without clinical symptoms and may require treatment. Although PARSABIV is cleared by dialysis, hemodialysis has not been studied as a treatment for PARSABIV overdosage. In the event of overdosage, corrected serum calcium should be checked and patients should be monitored for symptoms of hypocalcemia, and appropriate measures should be taken *[see Warnings and Precautions (5.1) in PARSABIV full prescribing information]*.

AMGEN®

PARSABIV™ (etelcalcetide)

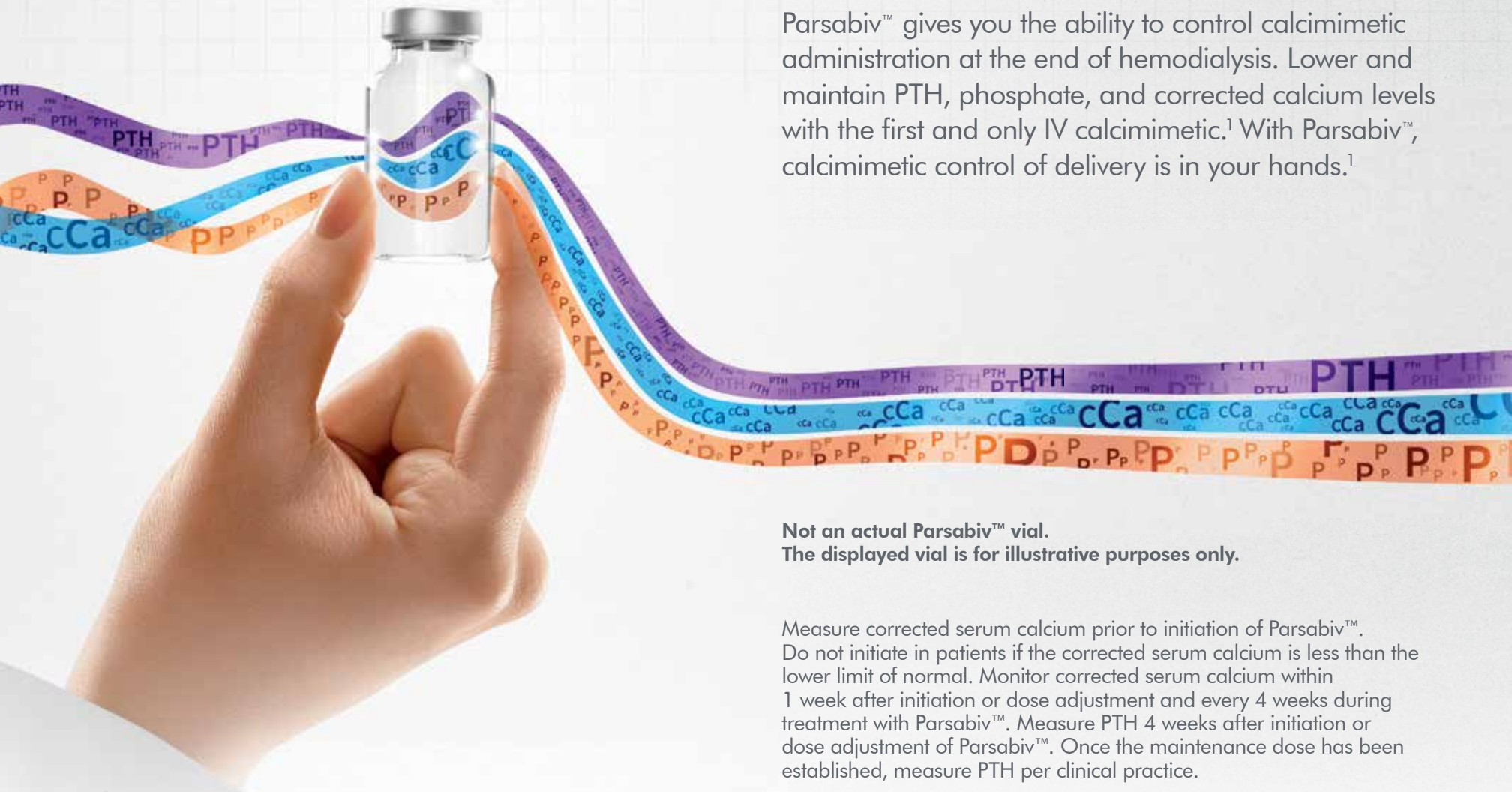
Manufactured for:
KAI Pharmaceuticals, Inc., a wholly owned subsidiary of Amgen, Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799

Patent: http://pat.amgen.com/Parsabiv/

02-17

Parsabiv™—

the control of calcimimetic delivery you've always wanted, the sustained lowering of sHPT lab values your patients deserve[1]



Parsabiv™ gives you the ability to control calcimimetic administration at the end of hemodialysis. Lower and maintain PTH, phosphate, and corrected calcium levels with the first and only IV calcimimetic.[1] With Parsabiv™, calcimimetic control of delivery is in your hands.[1]

Not an actual Parsabiv™ vial.
The displayed vial is for illustrative purposes only.

Indication

Parsabiv™ (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

Parsabiv™ has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Important Safety Information

Contraindication: Parsabiv™ is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred.

Hypocalcemia: Parsabiv™ lowers serum calcium and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia. Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Parsabiv™. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv™.

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv™. Monitor corrected serum calcium in patients with seizure disorders on Parsabiv™.

Concurrent administration of Parsabiv™ with another oral calcimimetic could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to Parsabiv™ should discontinue cinacalcet for at least 7 days prior to initiating Parsabiv™. Closely monitor corrected serum calcium in patients receiving Parsabiv™ and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of Parsabiv™. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv™. Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv™. Once the maintenance dose has been established, measure PTH per clinical practice.

Worsening Heart Failure: In Parsabiv™ clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv™ for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding: In clinical studies, 2 patients treated with Parsabiv™ in 1253 patient years of exposure had upper gastrointestinal (GI) bleeding at the time of death. The exact cause of GI bleeding in these patients is unknown and there were too few cases to determine whether these cases were related to Parsabiv™.

Patients with risk factors for upper GI bleeding, such as known gastritis, esophagitis, ulcers or severe vomiting, may be at increased risk for GI bleeding with Parsabiv™. Monitor patients for worsening of common Parsabiv™ GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Parsabiv™ therapy.

Adynamic Bone: Adynamic bone may develop if PTH levels are chronically suppressed.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Parsabiv™ to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

Please see Brief Summary of full Prescribing Information on adjacent page.

IV = intravenous; sHPT = secondary hyperparathyroidism; PTH = parathyroid hormone.

Reference: 1. Parsabiv™ (etelcalcetide) prescribing information, Amgen.

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Visit **ParsabivHCP.com** for more information.