

## New Blood Test Might Identify Calcification-Prone Patients



## By Tracy Hampton

Ithough vascular and soft tissue calcification can be deadly, physicians currently have no reliable tools for determining an individual's calcification risk. This is particularly pertinent to nephrologists and others who care for patients with compromised kidney function because pathologic vascular calcification has been called "the killer of patients with chronic kidney disease" (Mizobuchi M, et al. *J Am Soc Nephrol* 2009; 20:1453– 1464).

"We currently have quite a good idea about pathomechanisms triggering progressive calcification, and we think we know about a number of clinical factors predicting calcification progression including hyperphosphatemia, high calcium burden, and inflammation," said Markus Ketteler, MD, head of the division of nephrology at the University Hospital Würzburg, in Germany. "However, none of these factors shows a clear-cut linear relationship with the magnitude or progression of cardiovascular calcification or related events."

Now a newly developed nanoparticle-based test, which is described in a recent issue of the *Journal of the American Medical Association*, could change practice and provide an effective way to measure an individual's overall propensity for calcification in serum (Pasch A, et al. *J Am Soc Nephrol* doi: 10.1681/ ASN.2012030240 [published online ahead of print September 6, 2012]).

"This test may help to identify calcification-prone patients to guide and monitor their treatment. We regard this as an important step ahead in the field of calcification research and of potential importance for the treatment of patients with kidney disease worldwide," said first author Andreas Pasch, MD, of University Hospital and University of Bern, Inselspital, in Switzerland.

#### **Calculating calcification**

Calcifications in the body mainly consist of two components, calcium and phosphate, which combine to form calcium phosphate. Because calcium and phosphate concentrations in the blood are naturally near supersaturation, the balance of inhibitors and promoters of

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## **KIDNEY WEEK SCIENTIFIC SESSIONS**

#### **20 THURSDAY**

Tolerance and Kidney Transplantation Stare-of-the-Art Lecture: David H. Sachs

Sepsis AKI: Kidney as Amplifier and Target Robert W. Schrier Endowed Lectureship: Robert A. Star

Mutations in the K<sup>+</sup> Channel KCNJ5 Produce Primary Aldosteronism

Barry M. Brenner Endowed Lectureship: Richard P. Lifton

- 22 FRIDAY
  - Health Care Reform in America—Past, Present, and Future State-of-the-Art Lecture: William L. Roper

Renal Glucose Transport from Man to Molecule Homer W. Smith Address: Ernest M. Wright Stone Formation in Dent's Disease

Jack W. Coburn Endowed Lectureship: Rajesh V. Thakker Allocation of Health Care: Dialysis and Beyond

Christopher R. Blagg Endowed Lectureship: Bruce C. Vladeck

#### 26 SATURDAY

Entering the Era of Genomic Medicine: Research Opportunities and Challenges State-of-the Art Lecture: Eric D. Green

## 28 SUNDAY

Where Kidney Disease Was and Where It Is Headed State-of-the-Art Lecture: Robert W. Schrier

Podocyte Biology: The Key to Understanding Glomerular Disease Young Investigator Award: Tobias B. Huber



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## Calcification-Prone Patients

## Continued from page 1

these minerals critically influences the development of calcification. Under physiologic conditions, calcium and phosphate mineralize only in bones and teeth, but pathologic states can lead to soft tissue and vascular calcifications.

Intensive treatment, especially selfmedication with calcium-containing antacids and over-the-counter osteoporosis drugs, has led to a resurgence of the "milk alkali syndrome" associated with soft tissue calcifications and kidney damage. Also, patients with chronic kidney disease often have abnormally high blood calcium levels because of their compromised kidney function and metabolic insults of diabetes, dyslipidemia, oxidative stress, uremia, and hyperphosphatemia.

"Despite much progress in our molecular understanding of calcium homeostasis—particularly the role of the calcium-sensing receptor, renal phosphate handling, and epithelial calcium channels that are present in various tissues—the clinical determinants of pathologic calcifications are still incompletely understood," said Pasch. "Individual calcification risk cannot be determined, and patients particularly [likely] to develop calcifications cannot be identified."

Given the major clinical problem of accelerated calcification in many patients with chronic kidney disease, Pasch and his team set out to develop the first potentially widely available blood test that functionally integrates all the procalcification and anticalcification forces inherent in blood with one single measurement to obtain an estimate of the calcification propensity of individual serum samples.

The researchers found that when serum is artificially challenged with high amounts of calcium and phosphate, so-called primary calciprotein particles (CPPs) are formed. CPPs are proteinmineral aggregates that consist mainly of calcium, phosphate, and the two calcification-inhibiting serum proteins fetuin-A and albumin. Calcium and phosphate form an amorphous or colloidal state in primary CPPs, but with time, primary CPPs transform into secondary CPPs, which consist of a spectrum of proteins as well as crystalline (as opposed to colloidal) calcium phosphate. "The speed of transformation is a measure of calcification inhibition," Pasch said. "The longer the delay of transformation, the stronger the calcification-inhibiting forces in a given serum." In the presence of lower calcium and phosphate concentrations, CPP formation progresses only over weeks to months.

The transformation from primary CPPs, which are spherical, to secondary CPPs, which are spindle-shaped, causes turbidity that can be optically monitored with a commercial nephelometer, a photometer measuring scattered light. The test by Pasch and his team measures the kinetics of CPP transformation by detecting the changes in light scatter in a sample of serum. In its current format, the assay can measure approximately 200 serum samples per day.

## Getting to the clinic

To prove the test's utility, the researchers showed that in the presence of artificially elevated calcium and phosphate concentrations, their new nanoparticle-based assay detected the spontaneous transformation of primary CPPs to secondary CPPs. Also, the test found that both the sera of mice deficient in fetuin-A, a serum protein that inhibits calcification, and the sera of patients receiving hemodialysis had reduced intrinsic

properties to inhibit calcification. Blood from healthy volunteers did not.

"The test by Pasch et al. could show clear differences in calcification inhibitory capacity of calcification-prone fetuin-A knockout mice and dialysis patients versus wild-type mice and healthy volunteers, respectively," said Georg Schlieper, MD, an assistant professor at the RWTH Aachen University Hospital, in Germany. "This discrimination appears as a very promising approach in identifying patients at high risk for calcification and has the later potential to guide through decalcification therapy."

In other words, the test may also become an important tool for identifying and testing calcification inhibitors and may provide the basis for treatment monitoring in patients who receive such inhibitors.

Whereas the findings and their im-

plications are promising, "future experimental and clinical studies are essential in order to establish this calcification test for clinical use. These data need to be confirmed in patient cohorts in prospective studies, especially in conjunction with outcome parameters," Schlieper said.

Ketteler added that "in addition to systemic or circulating calcificationmodifying factors, there are some potent locally expressed and active calcification inhibitory systems at work—including matrix Gla protein, or MGP, and pyrophosphates—which may not be detected here."

The test in its current form requires strict temperature control and liquid handling. Further automation and simplification could help make the test more useful for basic and clinical research, the investigators said.

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ASN Kidney News is published by the American Society of Nephrology 1510 H Street NW, Suite 800, Washington, DC 20005. Phone: 202-640-4660

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Postmaster: Please send address changes to *ASN Kidney News*, c/o Customer Service, American Society of Nephrology 1510 H Street NW, Suite 800, Washington, DC 20005.

Publications mail agreement No. 40624074. Return undeliverable Canadian addresses to PO Box 503, RPO West Beaver Creek, Richmond Hill ON L4B 4R6

ASN Kidney News (ISSN print 1943-8044 and online 1943-8052) is an official publication of the American Society of Nephrology, 1510 H Street NW #800, Washington DC 20005, and is published monthly. Periodicals postage paid at Washington, DC and at additional mailing offices. Subscription rates: \$12 per year. To order, please email bhenkel@asn-online.org. Subscription prices subject to change. Annual ASN membership dues include \$12 for ASN Kidney News subscription. Copyright© 2012 All rights reserved

## Setting the Standard For Education: ASN Kidney Week and Beyond

Kidney Week 2012 includes several exciting new features and resources. The theme of the meeting, "Curing Kidney Disease," will be incorporated in the President's Address as well as in several oral abstract sessions via invited lectures. The lectures will address topics such as acute kidney injury, autoimmunity, channelopathies, diabetes, dialytic therapy, glomerulopathies, hypertension, lupus nephritis, polycystic kidney disease, and thrombotic microangiopathies.

## **Early Programs**

ASN offers 16 Early Programs on Tuesday, October 30, and/or Wednesday, October 31, preceding the Annual Meeting (November 1–4). New Early Programs are:

- Dialysis Facility Medical Directorship, covering all aspects of the roles and responsibilities of a medical director for a CMS-approved dialysis facility.
- Renal Relevant Radiology, covering the mechanistic bases of radiology techniques useful for the practicing nephrologist to improve selection and interpretation of ordered tests.

## **Diabetes Learning Pathway**

The new Diabetes Learning Pathway includes sessions on medical management, glycation, the renin–angiotensin system blockade, uric acid, and renal structure. The *Onsite Program* includes a list of all Learning Pathways and their associated sessions.

#### **High-Profile Oral Abstract Sessions**

The best abstracts from both regular and late-breaking submissions will be profiled in the following sessions:

- "Hot Science," scheduled for Friday, November 2, from 2 to 4 p.m., will feature abstracts focused on laboratory and translational science.
- "High Impact Clinical Studies," scheduled for Saturday, November 3, from 10:30 a.m. to 12:30 p.m., will highlight clinically focused abstracts, particularly clinical trials.

Each abstract presentation will be followed by audience questions, facilitated by session moderators.

## **Scientific Exposition**

A vital part of the Kidney Week educational experience is found on the scientific exposition floor, in Halls A/B/C of the convention center. New features include:

- Fellows Case Reports in the Posters Section feature clinical cases or pedigrees that demonstrate novel clinical findings; illustrate classic conditions in new or unusual ways; or illuminate and expand knowledge concerning physiology, cell biology, genetics, or molecular mechanisms.
- **Innovators Place** offers the opportunity for scientific discourse between medical device innovators and the nephrology community.
- The **Career Fair** allows attendees to meet face-to-face with representatives of top employers in the nephrology field—all in one place.

## Education and Membership for Nurses, Pharmacists, and Physician Assistants

Kidney Week 2012 attendance may convey eligibility for continuing medical education (CME) credits for physician assistants (PAs), continuing nursing education (CNE) credits for nurses, and continuing pharmacy education (CPE) credits for pharmacists. More information is available in the *Onsite Program*.

Nurses, pharmacists, and PAs who are not ASN members and who register for Kidney Week 2012 at the nonmember rate will receive complimentary ASN Affiliate Membership for 2013. Bring your registration receipt to the ASN Services Counter or Booth in the convention center to complete your membership application.

## ERRATUM

The September special section, *The Transition from Adolescent to Adult Care*, didn't acknowledge the efforts of editors Sandra Amaral, MD, MHS; Lorraine Bell, MD, FRCPC; and *ASN Kidney News* editorial board member Edgar Lerma, MD, FASN. This has been corrected in the online edition of *Kidney News* as of September 25, 2012. *ASN Kidney News* regrets the error and would like to recognize the contributions of Drs. Amaral, Bell, and Lerma to this important and timely work.



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## **ASN in Review**

During the last year, ASN continued to serve its 14,000 members and the kidney community worldwide, providing the best educational resources in nephrology, working with policymakers to improve kidney care, and adding exciting new programs that will advance research and patient care. The society is proud of its history of adding meaningful programs and member benefits every year to advance the careers and support the important achievements of kidney professionals worldwide.

## **Educating health professionals**

Since its inception, ASN has committed resources and expertise to providing the best professional education in nephrology. In the last year, ASN:

- Hosted the premier kidney meeting in the world in Philadelphia, helping more than 13,000 kidney professionals improve research and patient care.
- Added new features to Kidney Week 2012, including • Continuing education credits for nurses, phar
  - macists, and physician assistants • Launching ASN Innovators Place
- Adding an early program on dialysis facility management
- Offering the In-Service Exam as an early programExpanding the medical students and residents
- program at Kidney Week
  Expanding the employment opportunities through a career fair ar Kidney Week and online at ASN Career Center.
- Held regional meetings in Berlin, Chicago, Dallas, New York, Ouro Preto, Panama City, and Washington, DC, as well as held the Board Review Course and Update (BRCU) meeting.
- Continued expanding efforts to help nephrologists generate Maintenance of Certification (MOC) points through the Nephrology Self-Assessment Program (NephSAP) and Practice Improvement Modules (PIMs).
- Launched an onco-nephrology forum (http:// www.asn-online.org/about/committees/committee.aspx?panel=OncoNeph) to encourage and promote the exciting advances in this field.
- Expanded distance learning opportunities: ASN Highlights Online, BRCU Online, Kidney Week On-Demand, American Society of Transplantation/ASN Transplant Nephrology Core Curriculum, and the ASN Dialysis Curriculum.

## Advancing research and advocating the highest quality care for patients

Research is essential to improving kidney health, and nephrology is forging the path for changes in patient care that will affect many other areas of medicine. In the last year, ASN:

• Established the ASN Foundation for Kidney Research. The Foundation will raise funds to ensure continued support of innovative research in kidney disease. ASN created and funded the first fellowship, the Sharon Anderson Research Fellowship, in honor of the society's first female president.

- Launched a new program to foster the next generation of investigators who will help reach a cure for kidney disease. The ASN Research Fellowship Program funded nine new research fellows in 2012.
- Launched the William E. Mitch International Scholars Program to offer key support to international nephrology fellows and fellows from underrepresented minority groups.
- Launched the Kidney Health Initiative (KHI), an innovative program created in concert with FDA. Through KHI,



FDA. Through KHI, **KIDNEY HEALTH** INITIATIVE patient advocates and

kidney professionals will work with the FDA and industry groups to assess unmet needs in kidney treatment and evaluate the best options for developing new treatments that meet those needs.

- Coordinated ASN Hill Day 2012. More than 30 ASN leaders visited 60 congressional offices, informing congressional leaders about kidney health disparities and key advances in kidney care that require a sustained investment in research.
- Partnered with the American Kidney Fund, Dialysis Patient Citizens, the Urban League, and the American Society of Pediatric Nephrology to host congressional briefings on kidney health disparities and research in nephrology (see sidebar).

## Sharing new knowledge

ASN produces the most referenced, read, and respected kidney publications in the world. The society continues to provide a host of innovative approaches to providing key information to its members and the entire kidney community and to raising general public awareness of kidney health. In the last year, ASN:

- Participated in launching the American Board of Internal Medicine Foundation's Choosing Wisely campaign to help improve patient care. http://www.asnonline.org/policy\_and\_public\_affairs/choosingwisely/
- Selected the next Editor-in-Chief of the *Journal* of the American Society of Nephrology (JASN): Karl Nath, MD.
- Increased impact factor rankings (JASN, 9.663; Clinical Journal of the American Society of Nephrology, 5.227)
- Added mobile apps for *JASN* and *CJASN*, and mobile-friendly journal sites.
- Expanded ASN *Kidney News* readership to 41 countries.
- Redesigned its website to improve resources and features for ASN members.
- Produced educational films on geriatric nephrology care.
- Launched monthly video updates from the ASN Executive Director to help keep the kidney community informed.
- Developed resources to help physicians meet new meaningful use requirements regarding providing educational resources to patients.
- Increased the number of social media followers five-fold.

ASN looks forward to a successful annual meeting at Kidney Week 2012 and to the opportunity to continue to advance the interests of its members and the global kidney community in order to improve the care and lives of millions of patients with kidney disease.

## **ASN's Mission**

The American Society of Nephrology (ASN) leads the fight against kidney disease by educating health professionals, sharing new knowledge, advancing research, and advocating the highest quality care for patients.

## Focus on Health Disparities and Kidney Research

To advance research and advocate for the highest quality care for patients, ASN co-hosted two congressional briefings this year: on kidney health disparities and on research in nephrology.

In conjunction with the National Urban League and Dialysis Patient Citizens, ASN met with congressional staff and interested parties on April 19 at the "Kidney Health Disparities Briefing." Speakers included:

Kafui Agbemenu, MPH, MSN, RN

Health Advocate, Urban League of Greater Pittsburgh

Eric Edwards

Board of Directors, Dialysis Patient Citizens

Cristina M. Arce, MD

Division of Nephrology, Stanford University

*Neil R. Powe, MD* Chief of Medicine, San Francisco General

Hospital

Constance B. Wofsy

Distinguished Professor, University of California San Francisco

Dana Atwater, MBA

Account Executive, Baxter Healthcare

ASN co-hosted the June 19 briefing "Kidney Disease Research: From Concept to Cure," with the American Society of Pediatric Nephrology and the American Kidney Fund, with the Congressional Kidney Caucus as honorary cosponsor. Speakers included:

Griffin P. Rodgers, MD, MACP

Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Susan B. Shurin, MD Acting Director, National Heart Lung and Blood Institute (NHLBI)

LaVarne A. Burton

President and Chief Executive Officer, American Kidney Fund

H. William Schnaper, MD

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1) Katzman et al., J Vasc Surg 2009. 2) Gage et al., EJVES 2012. 3) Dageforde et al., JSR 2012. Indications for Use: The HeRO Graft is indicated for end stage renal disease patients on hemodialysis who have exhausted all other access options. See Instructions for Use for full indication, contraindication and caution statements. Rx only.

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# **President's Address**

## Launch of New Programs Marks 2012 Accomplishments

## An Interview with Ronald J. Falk, MD, FASN

## You have led ASN toward a number of new initiatives this year. One is the creation of the ASN Foundation for Kidney Research. Why does ASN need a foundation?

ASN needs a foundation to concentrate effort on support for kidney research. The society needs to develop funds for long-term preservation of fellowship programs, and the foundation allows industry and individuals to contribute to these important efforts.

Treatment will advance only if we train the next generation of researchers in kidney disease. These fellowships offer the best and the brightest the opportunity to concentrate two years of time on nephrology research, and they promote the long-term success of the young investigators who will help cure kidney disease.

## You spearheaded a new program called the Kidney Health Initiative (KHI). What is that?

The Kidney Health Initiative is a wonderful new program that allows the U.S. Food and Drug Administration (FDA), patient support groups, kidney organizations, and industry to work together to develop opportunities for drugs, devices, biologics, and food safety that benefit patients. Intuitively, everyone understands the potential of this partnership, a collaborative based on a similar effort in cardiovascular disease.

Kidney as a specialty has not produced adequate outcome measures or strongly encouraged new drug development and approval. Through a signed agreement with FDA, ASN can help rally the kidney community to overcome this gap. The Kidney Health Initiative encourages an iterative process in which all stakeholders work with the FDA to set appropriate guideposts for safe and beneficial development of drugs, devices, and biologics and for better food labeling.

## Why is food labeling important?

As I sit here today, I'm drinking a bottle of water. The water probably contains phosphorus, and may in fact have as much phosphorus as a glass of milk. It is essential for kidney patients to understand what they are ingesting. And the kidney community must do a better job of addressing food safety, including toxininduced kidney diseases such as hemolytic uremic syndrome.

## ASN is focusing more effort on promoting the concept of kidney professionals working "shoulder to shoulder." What does this mean?

In the practice domain physicians don't work in isolation. Physicians work with nurses, pharmacists, and physician assistants. These professionals work shoulder-to-shoulder to provide excellent care to patients with kidney disease. In the past, ASN focused its educational services on physicians, and as a society we now recognize the importance of educating the health care team. This is why ASN has expanded continuing education credits to allow all members of the kidney community to benefit professionally from attending the best nephrology meeting in the world.

#### You speak often about the joys of being a nephrologist. What do you find most satisfying when you see patients?

Being a nephrologist is a wonderful occupation. The patients we see have complex and fascinating problems that require astute insights and creative solutions. Nephrologists encounter a broad range of challenges, everything from transplants to stones to bone disease. The opportunity to care for these patients, to help someone get through a medical crisis and help restore their function, the opportunity to see someone recover so much quality of life after a transplant, or to help someone at the end of life die with dignity and respect—these are true privileges. It is for these kinds of opportunities that most of us went to medical school, and in helping our patients we make our own lives better.

## What is new at ASN Kidney Week 2012?

Among the new offerings at this meeting are a diabetes learning pathway that includes sessions on medical management, the renin–angiotensin system blockade, uric acid, and renal structure. In addition, this year's meeting provides an opportunity for trainees to present case reports. ASN has not encouraged case reports in the past, and I am really excited to learn more about what our trainees will share with us from their clinical experiences. More than 200 case reports will be presented at Kidney Week, and I encourage all meeting participants to visit these posters. This opportunity also helps nephrology training programs meet the requirements of the Accreditation

## The theme for Kidney Week 2012 is Curing Kidney Disease. You believe this specific phrase is important. Why?

Council for Graduate Medical Education.

Many other medical specialties use the word "cure" as a rallying cry, to highlight advances in their fields and to give patients hope. Kidney specialists hardly ever use that word, yet they work every day to restore patients' health and quality of life and to advance kidney research.

Historically, kidney professionals have employed poor word choices—"chronic," "progressive," "end-stage" that give a sense of poor outcomes. These words diminish the impressive accomplishments and many successes of the last 40 years, and our vocabulary doesn't reflect the positive changes this specialty has made in improving the lives of millions of patients.

## Will you still be able to conduct the Kidney Week podcast interviews this year?

Absolutely. I enjoy the interviews and learn so much from the people who share their meeting experiences with me.

## You have served on ASN Council for six years. What are ASN's most notable strengths?

Without question the ASN's greatest strength is its members. This community of professionals makes incredible contributions to medicine, science, and education. ASN's members benefit from the support of a phenomenally dedicated and experienced staff whose efforts allow members to have an effective voice in all areas of education, policy, and research. ASN's volunteer leaders bring a great sense of purpose to their work at ASN; their efforts reflect the immense contributions of the entire community.

Ronald J. Falk

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# Meet ASN's Next President

# Innovation and Translation to Top 2013 Agenda

Bruce A. Molitoris, MD, FASN, is Professor of Medicine and Director of the Indiana Center for Biological Microscopy at Indiana University. He graduated from the Washington University School of Medicine in St. Louis and completed his residency and fellowship training at the University of Colorado School of Medicine in Denver.

In addition to his work on ASN Council, Dr. Molitoris has chaired the ASN Kidney Week Program Committee, served on the ASN Training Program Directors Committee and the Nominating Committee, chaired the AKI Advisory Board, and played a central role in launching the ASN Workforce Committee. He has been involved in numerous NIH committees, NIH study sections, and National Kidney Foundation committees including the National Scientific Advisory Board.

The major area of his research studies over the last 25 years has centered on the cell biology of acute kidney injury, with an emphasis on proximal tubule cell injury secondary to ischemia and/or nephrotoxins. He also focuses on the use of 2-photon microscopy in live animals to understand the normal physiology, disease pathophysiology, and therapeutic responses. He has been continuously funded by both the NIH and the VA for over 25 years. He presently is the principal investigator of two NIH RO1s, P-30 O'Brien Core, a phase II STTR, a VA Merrit Review, and numerous industry grants. He is a founding member of two biotechnology companies dealing with 2-Photon and fluorescent technology.

## What are your areas of expertise in nephrology?

The two areas I enjoy most are acute kidney injury (AKI) and the use of intravital imaging to understand renal physiology and pathophysiology. Both areas are experiencing rapid and tremendous strides making this a very dynamic and exciting time. We have now expanded our use of imaging out beyond AKI into other areas where it has the tremendous opportunity to enhance our understanding of cell biologic processes and therapeutic mechanisms.

#### What made you decide to become a nephrologist?

I had always wanted to be an endocrinologist. Because I had a master's degree in nutrition from the University of Illinois, it was a natural progression toward endocrinology. I performed research with both endocrinologists and a nephrologist, Dr. Keith Hruska, during my medical school time at Washington University School of Medicine. I then went to the University of Colorado School of Medicine to work with a specific endocrinologist during my residency. However, after exposure to the outstanding nephrology faculty at the University of Colorado, I rapidly became enamored with both the acute care aspects of nephrology and also the tremendous opportunity to do the type of research I was interested in within nephrology. In particular, there was little going on in the cell biology of disease processes, and the physiology had been well worked out. This left an opening for a young nephrologist to create a career in an important basic science area with minimal competition, an opportunity I could not resist.

## You have been on ASN Council for five years. How do the leaders of ASN serve all 14,000 members?

ASN's goal is always to improve patient care whether through direct patient care, research, education, or public policy. An integrated network of MDs and PhDs comprise advisory groups, committees, strategic task forces, and the public policy board and provide expertise and guidance to the ASN Council on nearly all issues. The passion and dedication shown by these individuals exceeds my



expectations. An incredibly energetic, talented, and well coordinated ASN staff direct, assist, and facilitate all matters involving clinical, research, education, communication, and public policy aspects of what the ASN does. The ability of these individuals, and the particular structure now developed within the ASN executive director Tod Ibrahim's position, is an especially effective way to conduct an organization that interacts with all areas of nephrology. Since beginning on Council five years ago, the capabilities and contributions of all of these aspects of the leadership have been enhanced tremendously.

## How were you able to advance within the society to attain this position of leadership?

Advancement within the society is a difficult question to answer. In no way did I try to "advance," but I did try to serve ASN in a capacity in which I felt I could benefit the society. I was lucky in that my research had been successful and I was passionate about several areas within nephrology. My friend Dr. Norman Siegel invited me to be the Chair of the ASN Program Committee and I was identified as someone who could contribute. I would say the keys to recognition are to get involved in different ASN venues, do your job well, be positive, and be a consensus builder.

## What do you think ASN's primary focus should be over the next year?

It is hard to identify a "primary focus" for the ASN. I do like the way the Kidney Health Initiative (or "KHI") can be used as a focal point from which to foster and develop areas primarily benefiting patient care. This can involve direct patient care in the line of developing therapeutics, devices, and foods. It can also involve research leading to breakthroughs and translation to patient care, and it can involve education of physicians, health care workers, and the public at large. In working with the FDA, industry, and the NIH, ASN has an opportunity to focus on improving patient care at multiple sites. KHI is extremely exciting to me.

## What do you consider the most stimulating recent advances in nephrology?

There have been a number of recent advances in nephrology including the APOL1 susceptibility for focal segmental glomerular sclerosis (FSGS), anti-PLA2 receptor antibodies in membranous nephropathy, rapid advancement in AKI and CKD biomarkers, and the burgeoning therapeutic advances in preventing AKI and forestalling CKD. However, once an opportunity becomes a success, it is time to refocus on new opportunities and challenges that will benefit patients in either the short or long term. Nephrology is now experiencing a tremendous birth of excitement and interest by pharmaceutical companies as the opportunities listed

## Meet ASN's Next President

Continued from page 11

above offer unbelievable prospects for improving patient care and halting the progression to end stage renal disease. To do this, nephrology, with the ASN's help, must increase its scientific diversity and be open to scientific and clinical innovation and ideas.

The kidney is a vastly understudied organ when it comes to specific cellular and molecular processes because of the lack of public awareness of the importance of kidney disease and the lack of involvement of scientific disciplines outside of nephrology. We need to work hard to facilitate involvement of other scientific disciplines including immunology, cell and molecular biology, biomedical engineers, and many more outside the field of nephrology to apply their expertise to important processes that directly relate to kidney disease. This can take many forms including education but also should include research dollars for individuals working within these scientific areas to encourage them to study aspects of kidney diseases. Therefore, multidisciplinary educational and research programs and associated funding opportunities are necessary. Industry's focus on nephrology and a growing involvement of widely diverse scientific disciplines will pay major dividends in therapeutic success in the future.

#### If you could change one thing about kidney care, what would it be?

This is an easy question and one that I have pondered for some time. I believe public awareness of the importance of kidney disease is extremely low and needs to be dramatically enhanced. Although many attempts are being made to improve the situation, I believe one of the best ways to do this is a grass roots movement involving the public. Think about the cholesterol or blood pressure campaigns and their success. Until we do this, we will not receive the recognition necessary for the funding required to enhance disease detection and therapeutics for improving kidney disease patient care. This type of campaign is beyond the ASN, but it seems to me professional societies, patient support groups, the National Institutes of Health, and industry should come together around this need.

My greatest desires are to be able to identify those patients likely to develop kidney disease early and to be able to monitor them in ways that will allow appropriate therapies to be administered earlier than we are capable of doing today. I believe this is well within our reach and that's why the meeting will emphasize innovation, translation, and individualization as it relates to improving patient care at an early stage, thus minimizing the number of patients who require dialysis as a final therapy.

## What do you tell young people who are considering whether to study nephrology?

First I tell them that nephrology is not as difficult as they have been led to believe by medical school physiology. Nephrology is an extremely exciting clinical field and an equally exciting research field. The opportunities in nephrology research are the greatest within medicine subspecialties and are waiting for young, dynamic, and bright individuals to take up the cause. Clinical nephrology is also an exciting and rewarding area: we tend to overexpose our students and residents to extremely challenging patients with many comorbidities and underexpose students to the many successes of the transplant and outpatient areas. This question is directly tied into the next question involving the ASN Workforce Committee.

## You have been very closely involved with the creation of ASN's Workforce Committee. What do you consider the major workforce challenges in nephrology?

The challenges facing the ASN Workforce Committee are enormous and difficult to get your arms around. Surveys have informed us that medical students and residents see nephrology as too difficult intellectually, too demanding clinically, and not as rewarding as other medical subspecialty areas in terms of



patient-physician interactions. This has resulted in a steady decline over the last 10 years in the percentage of U.S. medical school graduates entering into nephrology fellowship programs from nearly 60 percent to almost 30 percent Although part of this percent decrease was due to an increase in the number of fellowship positions, it remains a concerning trend. To start to reverse this trend, an ASN taskforce was established to identify the areas requiring attention. Then the ASN Workforce Committee, under the outstanding leadership of Dr. Mark Parker and Dr.

Sharon Silbiger, was established. They have identified four major areas of concern:

- 1. Public awareness/web base activities
- 2. Faculty development
- 3. Curriculum coordination
- 4. Workforce diversity

One exciting program being expanded by support from the ASN is the Kidney Disease Screening and Awareness Program (KDSAP) started by Li-Li Hsiao at the Brigham and Women's Hospital. This program engages college students in a kidney disease screening program with the intention of exciting the students about a career in nephrology. This committee will continue to develop exciting opportunities in all of the areas outlined that will enhance the interest of and supply of future nephrologists.

## Do you recall your first ASN meeting, and what your impressions were of the society?

What I can recall, and it was such a long time ago, is that there seemed to be more parties and the amount of basic

# **Reducing the burden of ESA** administration

Consider the first once-monthly, non-EPO ESA offering less-frequent dose administration.

#### INDICATION AND LIMITATIONS OF USE

OMONTYS® (peginesatide) Injection is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis.

OMONTYS is not indicated and is not recommended for use in patients with CKD not on dialysis, in patients receiving treatment for cancer and whose anemia is not due to CKD, or as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia. OMONTYS has not been shown to improve symptoms, physical functioning, or health-related quality of life.

#### **IMPORTANT SAFETY INFORMATION**

WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE.

- Chronic Kidney Disease: In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.
- Use the lowest OMONTYS dose sufficient to reduce the need for red blood cell (RBC) transfusions.

#### Contraindications

OMONTYS is contraindicated in patients with uncontrolled hypertension.

#### Warnings and Precautions

Increased mortality, myocardial infarction, stroke, and thromboembolism:

 Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. Use caution in patients with coexistent cardiovascular disease and stroke. Patients with CKD and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular reactions and mortality than other patients. A rate of hemoglobin rise of >1 g/dL over 2 weeks may contribute to these risks

Reference: Schiller B, Doss S, De Cock E, Del Aguila MA, Nissenson AR. Costs of managing anemia with erythropoiesis-stimulating agents during hemodialysi a time and motion study. *Hemodial Int*. 2008;12(4):441-449.



 In controlled clinical trials of ESAs in patients with cancer, increased risk for death and serious adverse cardiovascular reactions was observed. These adverse reactions included myocardial infarction and stroke

- In controlled clinical trials of ESAs, ESAs increased the risk of death in patients undergoing coronary artery bypass graft surgery (CABG) and deep venous thrombosis (DVT) in patients undergoing orthopedic procedures
- In 2 trials of OMONTYS, patients with CKD not on dialysis experienced increased specific cardiovascular events

Increased mortality and/or increased risk of tumor progression or recurrence in patients with cancer: The safety and efficacy of OMONTYS have not been established for use in patients with anemia due to cancer chemotherapy. OMONTYS is not indicated

in patients with cancer receiving chemotherapy.  $\label{eq:Hypertension: OMONTYS is contraindicated in patients with$ uncontrolled hypertension. Appropriately control hypertension prior to initiation of and during treatment with OMONTYS. Reduce or withhold OMONTYS if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions

Lack or loss of response to OMONTYS: For lack or loss of hemoglobin response to OMONTYS, initiate a search for causative factors. If typical causes of lack or loss of hemoglobin response are excluded, evaluate for antibodies to peginesatide.

**Dialysis management:** Patients receiving OMONTYS may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis.

Laboratory monitoring: Evaluate transferrin saturation and serum ferritin prior to and during OMONTYS treatment. Administer supplemental iron therapy when serum ferritin is less than 100 mcg/L or when serum transferrin saturation is less than 20%

#### Adverse reactions The most common adverse reactions in clinical studies in patients with CKD on dialysis treated with OMONTYS were dyspnea, diarrhea, nausea, cough, and arteriovenous fistula site complication.

Please see accompanying Brief Summary.



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science to clinical science of nephrology was way weighted toward basic science. I think the changes made in the last 30 years have been for the benefit of the society, but more importantly for the benefit of the patient. In my opinion, nephrology has suffered from limited translation of its basic science understanding to clinical application. This now needs to be the focus of our society. Therefore, the meeting for 2013 will emphasize the importance of any opportunities for innovation and translation for improved patient care.

## What are your plans for the 2013 annual meeting?

This is an exciting and challenging time as one always wants to develop the best possible Kidney Week program. First and foremost, I selected Dr. Anupam Agarwal, Professor of Medicine and Director of Nephrology at the University of Alabama at Birmingham School of Medicine, as the program chair for the 2013 meeting. He has played the primary role in identifying talented members for the program committee and leading the charge to develop an outstanding program. The program committee will work synergistically with the postgraduate education committee to plan a balanced meeting. The emphasis of the program will be on refocusing on the patient and translating innovations to enhance patient care.

## **Help Avert Cuts to Research: Join ASN in Call** for Balanced Approach to **Deficit Reduction**

By Thomas H. Hostetter, MD

As needs your support SN needs your support to protect of the smartest investments our country can make.

Research generates jobs, stimulates the economy, and enables life-saving medical advances. If Congress doesn't act by January 2013, federal funding for NIH will be cut by 8.2 percent, eliminating up to 2300 NIH research grants.

We can't let these cuts happen. ASN has joined more than 3000 other organizations urging Congress to adopt a balanced approach to deficit reduction that would protect medical research and other essential federal programs like education, public safety, and infrastructure.

The society needs your help, too. Tell your Congressional representatives that cuts alone will not solve our federal budget problems.

Go to www.asn-online.org for all the tools to connect you with your members of Congress, including talking points and fact sheets.

Congress won't act unless they hear from constituents like you. I'm going to meet with my representatives. I urge you to join me.

Thomas H. Hostetter, MD, is ASN Public Policy Board Chair.

## **Policy Update**

## ESRD Quality Incentive Program: ASN Provides Feedback on CMS Proposals

## By Rachel Shaffer

he Centers for Medicare & Medicaid Services (CMS) released its annual set of proposed updates and additions to the Medicare End Stage Renal Disease (ESRD) program for public comment in July 2012. The ASN Quality Metrics Task Force and Public Policy Board spent the summer analyzing the proposed rule's potential impact on patient outcomes, access, and safety, and the integrity of the patient-physician relationship.

The society submitted feedback to CMS on August 31, 2012, emphasizing support for CMS' goal of monitoring access to and quality of dialysis care within a bundled payment system, and providing suggestions for improvement to the agency's proposals. ASN underscored the vital importance of only implementing measures that are substantiated by rigorous, scientifically validated evidence. ASN's complete comments are available online; this article summarizes some key conclusions from the task force.

Although ASN supported several of CMS' proposals related to the ESRD Quality Incentive Program (QIP), the society conveyed that, overall, the existing and proposed new measures for the QIP are not as relevant as others CMS might have suggested. Many measures focus on processes—such as monitoring and collecting data—rather than on outcomes that affect quality and value.

ASN encouraged CMS to ensure to the extent possible—that existing and future measures be applicable for patients who dialyze via peritoneal dialysis, home hemodialysis, and other treatment strategies including daily and nocturnal dialysis. The society also recommended that CMS consider adding metrics to evaluate appropriate referral for transplantation, as well as appropriate choice of palliative care.

ASN was most concerned regarding CMS' proposals to add a clinical hypercalcemia measure and to establish an overly ambitious performance standard for the percent of patients with a fistula. ASN also encouraged CMS not to implement its proposal to require facilities to report QIP data on 98 percent of patients, suggesting that a more reasonable alternative would be to consider only patients who received seven or more dialysis sessions per month eligible for QIP measures.

## **Mineral metabolism**

CMS proposed expansion of an existing mineral metabolism measure and adoption of a measure assessing the number of patients with uncorrected serum calcium >10.2 mg/dL. ASN recommended that CMS not implement these suggestions, emphasizing that insufficient evidence exists to substantiate a 10.2 mg/dL calcium level.

"The only evidence supporting this benchmark is observational data, which is not sufficiently rigorous to substantiate an incentivized measure. Implementing this measure would effectively cement a practice based on observation-



Brief Summary of Prescribing Information for: OMONTYS (peginesatide) Injection for intravenous or subcutaneous use

WARNING: ESAS INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE. See full prescribing information for complete boxed warning.

Chronic Kidney Disease:

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks [see Warnings and Precautions].
- Use the lowest OMONTYS dose sufficient to reduce the need for red blood cell (RBC) transfusions [see Warnings and Precautions].

#### INDICATIONS AND USAGE

#### Anemia Due to Chronic Kidney Disease

OMONTYS is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis.

Limitations of Use

- OMONTYS is not indicated and is not recommended for use:
  In patients with CKD not on dialysis because of safety concerns in this population [see Warnings and Precautions].
- In patients receiving treatment for cancer and whose anemia is not due to CKD, because ESAs have shown harm in some settings and the benefit-risk factors for OMONTYS in this setting have not been evaluated [see Warnings and Precautions].
- As a substitute for RBC transfusions in patients who require immediate correction of anemia.
- OMONTYS has not been shown to improve symptoms, physical functioning or health-related quality of life.
- CONTRAINDICATIONS

OMONTYS is contraindicated in patients with:

Uncontrolled hypertension [see Warnings and Precautions].

## WARNINGS AND PRECAUTIONS

### Increased Mortality, Myocardial Infarction, Stroke, and Thromboembolism

- In controlled clinical trials of other ESAs in patients with CKD comparing higher hemoglobin targets (13 14 g/dL) to lower targets (9 11.3 g/dL) (see Table 2), increased risk of death, myocardial infarction, stroke, congestive heart failure, thrombosis of hemodialysis vascular access, and other thromboembolic events was observed in the higher target groups.
- Using ESAs to target a hemoglobin level of greater than 11 g/dL increases the risk of serious adverse cardiovascular reactions and has not been shown to provide additional benefit. Use caution in patients with coexistent cardiovascular disease and stroke. Patients with CKD and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular reactions and mortality than other patients. A rate of hemoglobin rise of greater than 1 g/dL over 2 weeks may contribute to these risks.
- In controlled clinical trials of ESAs in patients with cancer, increased risk for death and serious adverse cardiovascular reactions was observed. These adverse reactions included myocardial infarction and stroke.
- In controlled clinical trials, ESAs increased the risk of death in patients undergoing coronary artery bypass graft surgery (CABG) and deep venous thrombosis (DVT) was observed in patients undergoing orthopedic procedures.
- The design and overall results of 3 large trials comparing higher and lower hemoglobin targets are shown in Table 2 (Normal Hematocrit Study (NHS), Correction of Hemoglobin Outcomes in Renal Insufficiency (CHOIR) and Trial to Reduce Cardiovascular Events with Aranesp<sup>®</sup> Therapy (TREAT)).

#### Table 2 Adverse Cardiovascular Outcomes in Randomized Controlled Trials Comparing Higher and Lower Hemoglobin Targets in Patients with CKD

	NHS (N = 1265)	CHOIR (N = 1432)	TREAT (N = 4038)			
<b>Time Period of Trial</b>	1993 to 1996	2003 to 2006	2004 to 2009			
Population	Patients with CKD on hemodialysis with coexisting CHF or CAD, hematocrit 30 ± 3% on epoetin alfa	Patients with CKD not on dialysis with hemoglobin < 11 g/dL not previously administered epoetin alfa	Patients with CKD not on dialysis with type II diabetes, hemoglobin ≤ 11 g/dL			
Hemoglobin Target; Higher vs. Lower (g/dL)	14.0 vs. 10.0	13.5 vs. 11.3	13.0 vs. ≥ 9.0			
Median (Q1, Q3) Achieved Hemoglobin level (g/dL)	12.6 (11.6, 13.3) vs. 10.3 (10.0, 10.7)	13.0 (12.2, 13.4) vs. 11.4 (11.1, 11.6)	12.5 (12.0, 12.8) vs. 10.6 (9.9, 11.3)			
Primary Endpoint	All-cause mortality or non-fatal MI	All-cause mortality, MI, hospitalization for CHF, or stroke	All-cause mortality, MI, myocardial ischemia, heart failure, and stroke			
Hazard Ratio or Relative Risk (95% CI)	1.28 (1.06 – 1.56)	1.34 (1.03 – 1.74)	1.05 (0.94 – 1.17)			
Adverse Outcome for Higher Target Group	All-cause mortality	All-cause mortality	Stroke			
Hazard Ratio or Relative Risk (95% CI)	1.27 (1.04 – 1.54)	1.48 (0.97 – 2.27)	1.92 (1.38 – 2.68)			

Patients with Chronic Kidney Disease Not on Dialysis

OMONTYS is not indicated and is not recommended for the treatment of anemia in patients with CKD who are not on dialysis.

A higher percentage of patients (22%) who received OMONTYS experienced a composite cardiovascular safety endpoint event compared to 17% who received darbepoetin alfa in two randomized, active-controlled, open-label, multi-center trials of 983 patients with anemia due to CKD who were not on dialysis. The trials had a pre-specified, prospective analysis of a composite safety endpoint consisting of death, myocardial infarction, stroke, or serious adverse events of congestive heart failure, unstable angina or arrhythmia (hazard ratio 1.32, 95% CI: 0.97, 1.81).

## Increased Mortality and/or Increased Risk of Tumor Progression or Recurrence in Patients with Cancer receiving ESAs

OMONTYS is not indicated and is not recommended for reduction of RBC transfusions in patients receiving treatment for cancer and whose anemia is not due to CKD because ESAs have shown harm in some settings and the benefit-risk factors for OMONTYS in this setting have not been evaluated.

The safety and efficacy of OMONTYS have not been evaluated. The safety and efficacy of OMONTYS have not been established for use in patients with anemia due to cancer chemotherapy. Results from clinical trials of ESAs in patients with anemia due to cancer therapy showed decreased locoregional control, progression-free survival and/or decreased overall survival. The findings were observed in clinical trials of other ESAs administered to patients with: breast cancer receiving chemotherapy, advanced head and neck cancer receiving radiation therapy, lymphoid malignancy, cervical cancer, non-small cell lung cancer, and with various malignancies who were not receiving chemotherapy or radiotherapy.

#### Hypertension

OMONTYS is contraindicated in patients with uncontrolled hypertension. Appropriately control hypertension prior to initiation of and during treatment with OMONTYS. Reduce or withhold OMONTYS if blood pressure becomes difficult to control. Advise patients of the importance of compliance with antihypertensive therapy and dietary restrictions.

#### Lack or Loss of Response to OMONTYS

For lack or loss of nesponse to OMONTYS, initiate a search for causative factors (e.g., iron deficiency, infection, inflammation, bleeding). If typical causes of lack or loss of hemoglobin response are excluded, evaluate the patient for the presence of antibodies to peginesatide. In the absence of antibodies to peginesatide, follow dosing recommendations for management of patients with an insufficient hemoglobin response to OMONTYS therapy. Contact Affymax, Inc. (1-855-466-6689) to perform assays for binding and neutralizing antibodies.

#### Dialysis Management

Patients may require adjustments in their dialysis prescriptions after initiation of OMONTYS. Patients receiving OMONTYS may require increased anticoagulation with heparin to prevent clotting of the extracorporeal circuit during hemodialysis. Laboratory Monitoring

Evaluate transferrin saturation and serum ferritin prior to and during OMONTYS treatment. Administer supplemental iron therapy when serum ferritin is less than 100 mcg/L or when serum transferrin saturation is less than 20%. The majority of patients with CKD will require supplemental iron during the course

al data, impeding further progress toward generating more evidence regarding an optimal calcium level. Moreover, virtually every dialysis facility already collects serum calcium and phosphorus concentrations," said task force chair Thomas H. Hostetter, MD. "Because compliance with this measure is already so widespread, expanded reporting to CMS that dialysis facilities collected the

data is unlikely to lead to improved patient care or outcomes."

#### Vascular access

ASN is committed to promoting patient access to the most appropriate type of vascular access, and was concerned that CMS proposed to set the bar too high for the number of patients with a fistula. The society urged CMS to reconsider its proposed standard to allow sufficient leeway between the maximum number of catheters and the minimum number of fistulas so as to not penalize facilities with patients who are appropriate candidates for grafts.

ASN suggested that CMS consider permitting patients who are not appropriate candidates for a fistula-owing to age, comorbid conditions, or limited

of ESA therapy. Following initiation of therapy and after each dose adjustment, monitor hemoglobin every 2 weeks until the hemoglobin is stable and sufficient to minimize the need for RBC transfusion. Thereafter, hemoglobin should be monitored at least monthly provided hemoglobin levels remain stable. ADVERSE REACTIONS

The following serious adverse reactions observed during clinical trials with OMONTYS are discussed in greater detail in other sections of the labeling Increased Mortality, Myocardial Infarction, Stroke, and Thromboembolism [see Warnings and Precautions]

- Hypertension [see Warnings and Precautions]

#### **Clinical Trials Experience**

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

#### Patients with Chronic Kidney Disease

Adverse reactions were determined based on pooled data from two active controlled studies of 1066 dialysis patients treated with OMONTYS and controlled studies of 1066 dialysis patients treated with OMONTYS and 542 treated with epoetin, including 938 exposed for at least 6 months and 825 exposed for greater than one year to OMONTYS. The population for OMONTYS was 20 to 93 years of age, 58.5% male, and the percentages of Caucasian, Black (including African Americans), and Asian patients were 57.9%, 37.4%, and 3.1%, respectively. The median weight adjusted dose of OMONTYS was 0.07mg/kg and 113 U/week/kg of epoetin.

Table 3 summarizes the most frequent adverse reactions ( $\geq$  10%) in dialysis patients treated with OMONTYS.

Table 3 Adverse Reactions Occurring in  ${\geq}10\%$  of Dialysis Patients treated with OMONTYS

Adverse Reactions	Dialysis Patients Treated with OMONTYS (N = 1066)	Dialysis Patients Treated with Epoetin (N = 542)	
Gastrointestinal Disorders			
Diarrhea	18.4%	15.9%	
Nausea	17.4%	19.6%	
Vomiting	15.3%	13.3%	
Respiratory, Thoracic and Media	astinal Disorders		
Dyspnea	18.4%	19.4%	
Cough	15.9%	16.6%	
Injury, Poisoning and Procedura	l Complications		
Arteriovenous Fistula Site Complication	16.1%	16.6%	
Procedural Hypotension	10.9%	12.5%	
Nervous System Disorders			
Headache	15.4%	15.9%	
Musculoskeletal and Connective	Tissue Disorders		
Muscle Spasms	15.3%	17.2%	
Pain in Extremity	10.9%	12.7%	
Back Pain	10.9%	11.3%	
Arthralgia	10.7%	9.8%	
Vascular Disorders			
Hypotension	14.2%	14.6%	
Hypertension	13.2%	11.4%	
General Disorders and Administ	ration Site Conditions	3	
Pyrexia	12.2%	14.0%	
Metabolism and Nutrition Disord	iers		
Hyperkalemia	11.4%	11.8%	
Infections and Infestations			
Upper Respiratory Tract Infection	11.0%	12.4%	

Seizures have occurred in patients participating in OMONTYS clinical studies. During the first several months following initiation of OMONTYS, blood pressure an presence of premonitory neurologic symptoms should be monitored closely. Advise patients to contact their healthcare practitioner for new-onset seizures, premonitory symptoms, or change in seizure frequency.

Allergic reactions have been reported in patients treated with OMONTYS. Discontinue OMONTYS and administer appropriate therapy if a serious allergic, anaphylactic or infusion-related reaction occurs.

#### Immunogenicity

Of the 2357 patients tested, 29 (1.2%) had detectable levels of peginesatidespecific binding antibodies. There was a higher incidence of peginesatide-specific

binding antibodies in patients dosed subcutaneously (1.9%) as compared to those dosed intravenously (0.7%). Peginesatide neutralizing antibodies were detected *in vitro* using a cell-based functional assay in 21 of these patients (0.9%). In approximately half of all antibody-positive patients, the presence of antibodies was associated with declining hemoglobin levels, the requirement for increased doses of OMONTYS to maintain hemoglobin levels, and/or transfusion for anemia of CKD. No cases of pure red cell aplasia (PRCA) developed in patients receiving OMONTYS during clinical trials.

#### DRUG INTERACTIONS

No formal drug/drug interaction studies have been performed. Peginesatide does not bind to serum albumin or lipoproteins as demonstrated in *in vitro* protein binding studies in rat, monkey and human sera. *In vitro* studies conducted with human hepatocytes or microsomes have shown no potential for peginesatide to induce or inhibit CYP450 enzymes.

#### **USE IN SPECIFIC POPULATIONS**

## Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Peginesatide was teratogenic and caused embryofetal lethality when administered to pregnant animals at doses and/or exposures that resulted in polycythemia. OMONTYS should be used during pregnancy only if the potential benefit justifies the notential risk to the fetue. benefit justifies the potential risk to the fetus.

Administration of peginesatide by intravenous injection to rats and rabbits during organogenesis was associated with embryofetal toxicity and malformations. Dosing was every third day in rats for a total of 5 doses and every fifth day in rabbits for a total of 3 doses (0.01 to 50 mg/kg/dose). In rats and rabbits, adverse embryofetal effects included reduced fetal weight, increased resorption, embryofetal toxicity was evident in rats and reduced ossification of sternebrae and metatarsals, and reduced ossification of some bones. Embryofetal toxicity was evident in rats at peginesatide doses of  $\geq 1$  mg/kg and the malformations (cleft palate and sternoschisis, and variations in blood vessels) were mostly evident at doses of  $\geq 10$  mg/kg. The dose of 1 mg/kg results in exposures (AUC) comparable to those in humans after intravenous administration at a dose of 0.35 mg/kg in patients on dialysis. In a separate embryofetal developmental study in rats, reduced fetal weight and reduced ossification in rabbits were observed at  $\geq 0.5$  mg/kg/dose of peginesatide. In a separate embryofetal developmental study in rabs, reduced at  $\geq 5$  mg/kg/dose of peginesatide. In a separate embryofetal developmental study in rabs, reduced to a set of a separate embryofetal exclose of 0.25 mg/kg. The dose of the metators were seen at a lower dose of 0.25 mg/kg. The dose of peginesatide. In a separate embryofetal developmental study in rabs, reduced at  $\geq 0.5$  mg/kg/dose of peginesatide. In a separate embryofetal developmental study in rabs, reduced to a set of the metators are set of the set of Administration of peginesatide by intravenous injection to rats and rabbits during peginesatide. In a separate embryofetal developmental study in rabbits, adverse findings were observed at lower doses and included increased incidence of fused sternebrae at 0.25 mg/kg. The effects in rabbits were observed at doses lower (5% - 50%) than the dose of 0.35 mg/kg in patients.

## **Nursing Mothers**

It is not known whether peginesatide is excreted in human milk. Because many drugs are excreted into human milk, caution should be exercised when OMONTYS is administered to a nursing woman.

## Pediatric Use

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

#### Geriatric Use

of the total number of dialysis patients in Phase 3 clinical studies of OMONTYS, 32.5% were age 65 and over, while 13% were age 75 and over. No overall differences in safety or effectiveness were observed between these subjects and vounger subjects.

#### OVERDOSAGE

OMONTYS overdosage can elevate hemoglobin levels above the desired level which should be managed with discontinuation or reduction of OMONTYS dosage and/or with phlebotomy, as clinically indicated. Cases of severe hypertension have been observed following overdose with ESAs [see Warnings and Precautions].

## PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide).

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For more detailed information, see the full prescribing information for OMONTYS at www.omontys.com or contact Takeda Pharmaceuticals America, Inc.

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March 2012 PEG096 R1

L-DSG-0312-4



life expectancy-to be excluded from the measure. This approach would help mitigate cherry-picking concerns for patients without fistulas.

#### **Dialysis adequacy**

CMS also proposed replacing a "dialysis adequacy" measure using urea reduction ratio with Kt/V. Although urea removal information is important, it does not provide the all-inclusive picture the phrase "dialysis adequacy" suggests. ASN suggested that the nephrology community collectively-including CMS-reframe the language that it uses to describe Kt/V, using an alternative term such as "urea removal." This terminology shift would help the nephrology community focus on more comprehensive ways to monitor and improve the overall adequacy of dialysis therapy.

#### Anemia management

CMS did not propose any changes to the existing anemia management measure; however, ASN recommended that CMS consider assessing hemoglobin/ hematocrit levels on a rolling 3-month or 6-month basis rather than assessing the levels on a monthly basis. Assessing a single value per month has limited clinical utility or insight into the quality of care that an individual patient receives in a dialysis facility. A longer assessment period would provide a more complete picture of patients' overall anemia management.

## Standardized hospitalization ratio

A standardized hospitalization ratio is one measure CMS is considering adding to the QIP in future years. However, ASN is concerned that this measure could make it challenging for patients with multiple comorbid conditions or generally compromised health to gain admission to a dialysis unit. The task force also concluded that it is currently impossible to accurately case-mix adjust for changes in patients' comorbid conditions unrelated to dialysis. ASN suggested that CMS not implement the measure at this time, and at a minimum, pilot it before applying it to the entire ESRD patient population to assess whether these serious issues can be addressed.

"Hopefully, CMS will find ASN's feedback informative and useful as it continues to develop the QIP," Hostetter said. "A robust system assessing the accessibility and quality of dialysis services is critically important for our patients. Many challenges remain in developing an evidence-based system that accurately reflects the level of care offered, and ASN looks forward to continued interaction with CMS to make progress in this arena."

## **Policy Update**

## No Laughing Matter: Painful Budget Cuts Planned

By Grant Olan

n Friday, September 14, 2012, the White House Office of Management and Budget (OMB) released a highly anticipated report on the likely effects of sequestration (the automatic across-the-board cuts of \$1.2 trillion passed as part of the Budget Control Act in 2011 that are slated to take effect beginning January 2013). The report confirmed what everyone already knew—sequestration would bring massive budget cuts that would devastate federal programs.

Sequestration would reduce funding for the National Institutes of Health (NIH) by \$2.5 billion in FY 2013, or 8.2 percent, eliminating up to 2300 NIH research grants. NIH "would have to halt or curtail scientific research, including needed research into cancer and childhood diseases," the White House said.

Moreover, Medicare would face a 2 percent cut of \$11 billion, costing up to 766,000 jobs. The Centers for Medicare & Medicaid Services (CMS), which has much of the federal responsibility for implementing the 2010 Patient Protection and Affordable Care Act, would take a \$63 million hit to its program management budget. The prevention fund that the 2010 health care law created would be sliced by 7.6 percent, or \$76 million. Grants to states to create health insurance exchanges would be cut by \$66 million.

The OMB report said that "on the nondefense side, sequestration would undermine investments vital to economic growth, threaten the safety and security of the American people, and cause severe harm to programs that benefit the middle class, seniors, and children." Nondefense discretionary (NDD) spending funds essential government programs such as medical research, education, public safety, and infrastructure.

The goal of the NDD community is to speak with one voice in educating policymakers and the public about what NDD programs are as well as what the nation will stand to lose as a result of sequestration, and to encourage Congress to take a balanced approach of cuts and new revenue as it works toward a budget deal to replace sequestration.

"We can't just cut our way out of debt. Eliminating all NDD programs will not balance the budget and is not the answer," ASN Research Advocacy Committee Chair John R. Sedor, MD, said. "ASN knows medical research generates jobs, stimulates the economy, and enables life-saving medical advancements. That is why the society has joined more than 3000 national, state, and local organizations, including other medical specialty societies and research organizations, to raise awareness of and build support for federal NDD programs."

ASN has been collaborating with the NDD community in a number of ways. In July 2012, ASN joined the "Rally to Restore Balance and Protect America's Families" on Capitol Hill for the formal launch of the NDD campaign with Sen. Tom Harkin, Sen. Patty Murray (D-WA), Rep. Rosa DeLauro, (D-CT) Rep. George Miller (D-CA), and Phoenix Mayor Greg Stanton.

ASN joined the NDD community in calling upon Congress for a balanced approach to deficit reduction in July, and participated in an NDD community-wide national action day in September. ASN members were asked to Tweet or call their congressional representatives. Throughout the fall ASN will join the NDD community for congressional briefings and various meetings on Capitol Hill.

In addition to these NDD activities, the society offers a toolkit at www.asnonline.org to help ASN members meet with their congressional representatives in their home offices in November and December, including talking points and fact sheets.

Currently, there is no serious plan in Congress to repeal or replace sequestration. Instead, Congress has tacitly agreed to table this issue until after the November election, which is why ASN





members are being asked to meet with their representatives in Congress during the lame-duck session. What Congress decides to do is anyone's guess at this time. What happens largely depends on the outcome of the election and the balance of power in Washington. The hope, however, is that the combined efforts of the entire NDD community will generate enough support for replacing sequestration with a more balanced approach to deficit reduction that includes new revenues.



## **Submit Applications for Research Funding**

Basic science and clinical research advances patient care. ASN encourages you to submit your innovative ideas and research plans to the following programs.

**ASN Research Fellowships** provide funding to nephrology fellows for original and meritorious research, conducted under the guidance of a sponsor.

**ASN Career Development Grants** help new investigators conduct independent research.

Online applications for ASN Research Fellowships and ASN Career Development Grants opened October 15, 2012. The deadline to apply is Friday, December 14, 2012 at 4:00 p.m. EST.

For details and online applications, please visit the ASN website: http://www.asn-online.org/grants\_and\_funding/

## ASN Leads the Way to Innovation Center

Promote more patient-centered care. Include patients with end stage renal disease as well as later stages of chronic kidney disease. Allow a diversity of dialysis provider sizes and types to participate.

These are among the suggestions for a potential nephrology integrated care delivery model pilot program that ASNjoined by eight other patient and health professional organizations-discussed with leadership from the Centers for Medicare & Medicaid Services (CMS) and the CMS Innovation Center at CMS headquarters in early September (Table 1). Although CMS and the Innovation Center have not formally announced any plans for a nephrology integrated care delivery model pilot program or demonstration project, ASN and the other participants commended them for their interest in examining strategies to improve care and reduce costs for patients with kidney disease and voiced strong support for such a program.

In addition to thanking CMS administrator Jonathan Blum, Innovation Center Acting Director Richard Gilfillan, MD, and their staffs for their consideration of a pilot project focused on patients with kidney disease, ASN and the other groups provided recommendations for key considerations the agency should take into account to ensure the success of a pilot project and yield the most meaningful improvements for patients.

Although CMS and the Innovation Center are still considering the project, at this time, it is generally anticipated that a pilot program would likely entail a dialysis provider assuming responsibility for the care of a set number of patients with kidney disease, developing innovative ways of delivering and improving care for them, and having the opportunity to share in savings or receive a bonus payment from CMS for meeting certain quality metrics.

One theme that ASN and the other participating patient and health professional groups emphasized was the importance of considering including late-stage CKD patients—as well as patients with ESRD—in a pilot program. Improving care coordination and enhancing access at that stage could provide significant patient benefit, through means such as establishing appropriate vascular access, selecting the optimal modality, and arranging for nutritional supplements. It could also help defray costs, such as by reducing the number of patients who "crash" into dialysis in the emergency room, or have increased morbidity and mortality due to catheter infections.

Among the challenges to including this population are how to define "late stage CKD," and whether it is possible to involve patients with CKD who are not yet Medicare beneficiaries. Yet CMS and the Innovation Center possess a unique opportunity to profoundly transform care for patients with kidney disease, and ASN hopes the agency will engage with the nephrology community to develop creative solutions.

Other suggestions that participants in the meeting encouraged Mr. Blum, Dr. Gilfillan, and their staffs to consider included:

- Prospectively specifying the evaluation methodology that will be used to define success or failure.
- Improving patient access to transplantation, including pre-emptive transplantation.
- Including a role for patient peer mentoring.
- Incentivizing timely placement of appropriate vascular accesses.
- Allowing provider organizations that are large and small, and for-profit and non-profit, to participate.
- Utilizing the patients' time during incenter dialysis treatments to coordinate care for other comorbidities, such as heart disease or diabetes, and to provide educational interventions.

"Overall, I think that ASN and the other patient and health professional groups thought it was a constructive, interactive meeting, and sincerely appreciated CMS and the Innovation Center's consideration of the ideas our groups presented," said L. Lee Hamm, ASN Accountable Care Organization Task Force Chair, who represented ASN at the meeting. "Accounting for the perspectives and experiences of these two key constituencies in the design of a pilot program will be important for CMS and the Innovation Center to ensure its success. We all look forward to continuing the dialogue with them to capitalize on this exciting opportunity to improve care for our patients."

 Table 1. Patient and health professional organization participants in

 meeting with CMS and the Innovation Center

- American Association of Kidney Patients
- American Kidney Fund
- American Nephrology Nurses Association
- American Society of Nephrology
- American Society of Pediatric Nephrology
- Dialysis Patient Citizens
- National Kidney Foundation
- Renal Physicians Association
- Renal Support Network

## Announcing the ASN Foundation For Kidney Research

"Only through innovative research will the kidney community continue to implement advances that improve the lives of kidney patients and cure kidney disease."

> —American Society of Nephrology President Ronald J. Falk, MD, FASN



he American Society of Nephrology established the ASN Foundation for Kidney Research in March 2012 with one mission: to prevent and cure kidney diseases through research and innovation.

The foundation's first goal is to establish sustained funding to support the research of 20 fellows a year (10 with initial funding and 10 with continued funding). "This \$20 million commitment to nephrology ensures support to the next generation of researchers for years to come," said ASN President Ronald J. Falk, MD, FASN.

The first organization to contribute and help the foundation accomplish this goal was Fresenius Medical Care, which contributed \$10 million to establish the Ben J. Lipps Research Fellowship Program. This program will fund 10 new research fellows annually at \$50,000 for up to two years, including five Ben J. Lipps Research Fellows. The program also includes:

- The Sharon Anderson Research Fellowship, funded annually through a \$2 million donation from ASN to honor its first female president.
- The George B. Rathmann Research Fellowship, funded every other year through a \$1 million educational donation from Amgen.

With a combined \$13 million in funding, the foundation strives to reach its \$20 million goal by ASN's 50th anniversary in 2016.

ASN announced its commitment to fund research fellows in 2011. Out of 68 applicants, ASN awarded nine fellows with research funding beginning on Sunday, July 1, 2012. This year's program was partially funded by Amgen, Global Exposition Specialists (GES), Reata Pharmaceuticals, and Sanofi.

The ASN Foundation for Kidney Research is committed to maintaining and expanding this important program. The foundation welcomes the input of new partners and contributors to its research mission.

"Rates of kidney disease and kidney failure are rising globally, affect millions, and will increase in concert with the rise in major underlying causes: diabetes, hypertension, and obesity," said Dr. Falk, adding that the foundation is proud to contribute to the role medical and scientific research plays in improving human health.

Dr. Falk will announce the establishment of the ASN Foundation for Kidney Research—as well as the Ben J. Lipps Research Fellowship Program and the Ben J. Lipps Research Fellows, the Sharon Anderson Research Fellowship, and the George B. Rathmann Research Fellowship—during the Opening Plenary Session at ASN Kidney Week 2012 on Thursday, November 1, in San Diego.

## Effect of Quality Improvement Interventions on Health **Disparities Unclear**

A re quality improvement interven-tions effective at reducing disparities in health care? It's not clear, according to a recent literature review by the Agency for Healthcare Research and Quality. The analysis included articles from 1983 to 2011, and the reviewers looked for studies that evaluated the effect of strategies on disparities in the prevention or treatment of asthma, breast and

**Foundation**<sup>®</sup>

colorectal cancers, cardiovascular disease, cystic fibrosis, depression, diabetes, end stage renal disease (ESRD), pneumonia, and pregnancy.

"The most striking finding of the AHRQ report to me is that only 19 studies met the criteria for evidencebased quality improvement interventions to reduce health disparities in a broad population of conditions. This is a very low number," said Emory University School of Medicine's Rachel Patzer, PhD, MPH, an expert in transplant disparities. "There is little evidence to guide quality improvement strategies to reduce disparities, and it is clear that more research studies on quality improvement interventions are needed."

## **Limited information**

The 19 articles in the review rep-

resented 14 studies of cancer, cardiovascular disease, depression, and diabetes. Although the investigators did not find any studies that assessed quality improvement interventions in the kidney failure population that met their inclusion criteria, the findings in many ways apply to kidney care. Fourteen articles targeted or described disparities associated with differences in race or ethnicity, three pertained to socioeconomic status, two related to insurance status, two related to language, one dealt with health literacy, and one pertained to sex.

"I think it's helpful to look at other successful quality improvement interventions in other fields or diseases to see what may work in kidney disease," Patzer said.

Most interventions included education of patients and health care providers, although the specific approaches differed substantially across the studies. Overall, quality improvement interventions were not shown to reduce disparities, but the authors noted that the review should not be construed to assess the general effectiveness of quality improvement in the health care setting.

One challenge in conducting a systematic review in this area is the breadth and heterogeneity of clinical conditions, populations with the clinical conditions, quality improvement intervention strategies, and clinical outcomes. Compounding this heterogeneity are challenges to indexing quality improvement strategies in the medical literature.

## **Reducing disparities in kidney** care

Despite a vast number of research studies that have documented the existence of health disparities in kidney disease, there seem to be few evidence-based quality improvement interventions to reduce health disparities among kidney disease patients, Patzer said.

The lack of large-scale quality improvement interventions is due in part to the disconnect between community partners and researchers. "A population-based, regionally coordinated intervention would have the highest impact on health disparities," Patzer said. "It's important for researchers to work with community members to ensure that the quality improvement initiatives are conducted in a way that provides sufficient evidence, such as ensuring an adequate comparison group to evaluate effectiveness,"

"I think the kidney disease community should see this as a call to action for collaboration on quality improvement initiatives to reduce health disparities among kidney disease patients." Patzer said.





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# **ASN SCIENTIFIC EXPOSITION**

## Thursday, November 1 – Saturday, November 3 9:30 a.m. – 2:30 p.m.

## **Highlights Include:**

- Over 130 Exhibiting Companies
- ASN Services
  - CME Information, General Information, Membership Services, Publications, NephSAP, Foundation and Web Services
- Career Fair New! The Kidney Week Career Fair is an opportunity to meet face to face with professionals from around the country.
- **Complimentary Refreshment Breaks**
- Cyber Center
- **Exhibitor Spotlights**
- Innovators Place New! Innovators Place is designed to offer the opportunity for scientific discourse between medical device innovators and the nephrology community.
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## Exhibitor Spotlights

ASN has built a special theater in the scientific exposition hall to spotlight industry's latest advances in nephrology practices, products, services, and technologies during 60 minute presentations (no continuing medical education credit). Seating is first come, first served and limited to 75 participants.

All presentations include breakfast (morning presentations) or lunch (afternoon presentations).

## Schedule

## Thursday, November 1

10:00 a.m. - 11:00 a.m.

Glucose and Peritoneal Dialysis: Getting to the Heart of the Matter

Presented by **Baxter** 

12:30 p.m. – 1:30 p.m. The Risks and Clinical Consequences of Secondary Hyperparathyroidism

Otsuka



## Friday, November 2

10:00 a.m. - 11:00 a.m. Understanding and Managing Hyponatremia: A Specific Approach to Treatment

Presented by

Otsuka America Pharmaceutical, Inc.

## 12:30 p.m. – 1:30 p.m.

Rituxan for the Treatment of Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA)

Presented by Genentech





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## **Plenary Session**

Transplantation Tolerance Pioneer to Decribe Progress in Preventing Rejection



David H. Sachs

tate-of-the-Art Lectu

"Colerance and Kidney Transplantation" is the title of the state-of-the-art lecture to be delivered on Thursday, Nov. 1. Transplant tolerance researcher David H. Sachs, MD, is the speaker.

Dr. Sachs is director of the Transplantation Biology Research Center at Massachusetts General Hospital and the Paul S. Russell/Warner-Lambert Professor of Surgery (Immunology) at Harvard Medical School in Boston.

Two of the major limitations in the field of transplantation today are complications from the drugs used to prevent acute rejection and chronic

rejection, which causes the loss of some 5 percent of transplanted organs per year. Dr. Sachs has been active in exploring methods for inducing transplantation tolerance in order to avoid acute and chronic rejection without the need for long-term immunosuppressive medications. He will describe the work of his laboratory on the mechanisms involved in transplantation immunity at the basic level.

Dr. Sachs has published more than 700 articles in scientific journals. His research achievements include the development of monoclonal antibodies to major histocompatibility complex antigens, development of a unique large animal model for transplantation using miniature swine, use of mixed marrow reconstitution as a means of inducing specific tolerance, and studies of specific transplantation tolerance to allografts and xenografts in murine, swine, and primate models.

Dr. Sachs received his MD from Harvard Medical School and then was a surgical resident at the Massachusetts General Hospital from 1968 to 1970. He moved to the National Institutes of Health in Bethesda, MD, where he developed a major program in transplantation research. He became chief of the immunology branch of the National Cancer Institute in 1982, where he stayed until returning to Harvard in 1991.

He is one of the three North American editors of *Transplantation* and was the founding editor of *Xenotransplantation*. He has served the Transplantation Society as councilor and vice president for several terms. He was elected to the Institute of Medicine of the National Academy of Sciences in 1996. He has

received the Jean Borel Award in Transplantation, the ASTP/ Novartis Established Investigator Award, the Medical Foundation Award, the Roche AST Distinguished Achievement Award, and the Martin Prize for Excellence in Clinical Research. He holds an honorary degree from the University of Nantes, France.

## NIH Researcher Examines Sepsis and Acute Kidney Injury in Schrier Lectureship



he complex relationship between sepsis and acute kidney injury will be examined in the Robert W. Schrier Endowed Lectureship, titled, "Sepsis AKI: Kidney as Amplifier and Target," on Thursday, Nov. 1, at 2 p.m.

The speaker will be Robert A. Star, MD, director of the Division of Kidney, Urologic, and Hematologic Diseases at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). He is also a senior investigator and chief

Robert A. Star

of the renal diagnostics and therapeutics unit at the NIDDK.

Dr. Star has a particular interest in translational research. His laboratory focuses on the early identification, prevention, and preemption of sepsis and acute kidney injury. His research has produced more than 120 published manuscripts. He has written eight textbook chapters and holds several patents.

Dr. Star was a postdoctoral fellow at the National Institutes of Health (NIH) in the mid-1980s before joining the faculty of the University of Texas Southwestern Medical Center in Dallas. In 1999, he returned to NIH as a senior scientific advisor for kidney disease and to run a lab studying acute kidney injury. In 2002, he became senior advisor for clinical research in the NIH Office of Science Policy and Planning, where he worked on the NIH roadmap for medical research initiatives to re-engineer the clinical research enterprise. The roadmap aims to stimulate research and develop resources for cross-cutting, large, and complex projects with profound potential impact. He also led training and career programs for clinical researchers and helped develop the clinical and translational science awards.

Dr. Star graduated summa cum laude in applied mathematics from Harvard College and cum laude from the Harvard Medical School– Massachusetts Institute of Technology Joint Program in Health Sciences and Technology. His internship and residency in internal medicine were performed at Michael Reese Hospital in Chicago.

Dr. Star has received honorary awards and research support from NIH and the U.S. Food and Drug Administration. He received the Young Investigator Award recognizing excellence in nephrology research, jointly awarded by the American Society of Nephrology and the American Heart Association.

ASN gratefully acknowledges Otsuka America Pharmaceutical, Novartis, Astellas Pharma US, and several individuals for support of the Robert W. Schrier Endowed Lectureship.

## Brenner Lectureship to Cover Mutations that Produce Aldosteronism

esearch showing that somatic muta-

tions in a gene encoding a potassium

channel lead to 40 percent of aldos-

terone-producing adenomas in the adrenal

gland, a common cause of severe hypertension

worldwide, will be the subject of the Barry M.

Brenner Endowed Lectureship on Thursday,

Nov. 1, at 2 p.m. Richard P. Lifton, MD, PhD,

will speak on "Mutations in the K<sup>+</sup> Channel

Dr. Lifton is Sterling Professor of Genet-

ics and Internal Medicine, chair of the genet-

ics department, executive director of the Yale

Center for Genome Analysis, and investigator

at the Howard Hughes Medical Institute at

KCNJ5 Produce Primary Aldosteronism."



Richard P. Lifton

Yale University School of Medicine in New Haven, CT. Dr. Lifton completed his clinical training in internal medicine at Brigham and Women's Hospital in Boston, served as chief medical resident there, and continued on the faculty at Harvard Medical School before being recruited to Yale in 1993.

Dr. Lifton's team used a DNA sequencing strategy called whole exome sequencing to sequence all 23,000 human genes in DNA from adrenal adenomas from four patients. They compared those sequences to each patient's own blood-cell DNA, searching for mutations that had occurred somatically in the tumors. They found very few protein-altering somatic mutations, only about two per tumor. However, a gene encoding the KCNJ5 potassium channel was mutated twice. When the researchers studied other aldosterone-producing adenomas, they found one of the two mutations in KCNJ5 present in nearly 40 percent of them. These mutations alter the selectivity filter of the channel, allowing the passage of sodium into the cells. The resulting cell depolarization leads to increased intracellular calcium, the signal for aldosterone secretion and cell proliferation.

Dr. Lifton says that these findings reveal a surprisingly simple biology for the adrenal tumors and raise the possibility of developing a screening test to identify patients with these tumors by finding one of these two mutations in cells or tumor DNA in the blood.

Dr. Lifton has been a pioneer in using human genetics and genomics to identify more than 35 disease genes involved in key pathways underlying common diseases, including hypertension, myocardial infarction, osteoporosis, cerebral hemorrhage, congenital heart disease, and neoplasia. In the case of hypertension, these studies have led to new approaches to treatment and prevention strategies for the general population. His group recently developed a method for rapidly and inexpensively sequencing all the genes in the genome that is being widely used for disease gene discovery and clinical diagnosis.

Dr. Lifton is an elected member of the National Academy of Sciences and the Institute of Medicine. He chairs the scientific advisory board of Merck Pharmaceuticals and is a member of the governing councils of the Institute of Medicine, Association of American Physicians, and Coalition for the Life Sciences.

He has received the highest scientific awards of the American Society of Nephrology, Council for High Blood Pressure Research, American Society of Hypertension, American Heart Association, International Society of Hypertension, and International Society of Nephrology. He received the Wiley Prize for Biomedical Sciences in 2008.

ASN gratefully acknowledges Monarch Pharmaceuticals for support of the Barry M. Brenner Endowed Lectureship.

ASN congratulates 2012 award recipients			
	Thomas D. <b>DuBose</b> Jr., MD, FASN John P. Peters Award recipient	Nathan W. <b>Levin</b> , MD	Belding H. Scribner Award recipient
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	For more information about these awards or how to nominate a candidate	ate, please visit www.asn-online.or	rg/awards.

## **Plenary Session**

## State-of-the-Art Lecture Explores Future of Health Care Reform



William L. Roper

ealth care reform remains one of the hottest issues of the day, so an expert who has seen the system from many angles in a multifaceted career will share his insights into what lies ahead in the state-of-theart lecture on Friday, Nov. 2. A medical school dean, former health care company executive, and former high-level government official, William L. Roper, MD, MPH, has a unique perspective to share in his address, "Health Care Reform in America-Past, Present, and Future."

Dr. Roper is dean of the school of medicine and vice chancellor for medical affairs at the University of North Carolina at Chapel Hill (UNC) and chief executive officer of the UNC Health Care System. He also is professor of health policy and administration in the School of Public Health and professor of pediatrics and of social medicine in the School of Medicine at UNC. He was dean of the UNC School of Public Health from 1997 to 2004.

Before joining UNC in 1997, Dr. Roper was senior vice president of Prudential HealthCare. He joined Prudential in 1993 as president of the Prudential Center for Health Care Research.

Dr. Roper was director of the U.S. Centers for Disease Control and Prevention from 1990 to 1993, a member of the senior White House staff from 1989 to 1990, and administrator of the Health Care Financing Administration (now the Centers for Medicare & Medicaid Services) from 1986 to 1989. He has also been a White House fellow.

He received his medical degree and his masters from the University of Alabama at Birmingham. He completed his residency in pediatrics at the University of Colorado Medical Center.

Dr. Roper is a member of the Institute of Medicine of the National Academy of Sciences. He is a member of the board of directors of DaVita, Inc.; a member of the board of directors of Express Scripts, Inc., a company that handles millions of prescriptions through home delivery and at retail pharmacies; a member of the Scientific Management Review Board of the National Institutes of Health; a member of the board of directors of the Partnership for a Healthier America, a nonprofit organization devoted to working with the private sector to address childhood obesity; and chair of the board of directors of the National Quality Forum, a private sector, consensus-standard-setting organization aimed at health care performance measurement.

## Pioneer in Active Sodium Glucose Transporter Research to Receive Smith Award



Ernest M. Wright

physiology at UCLA in 1967.

A cclaimed investigator Ernest M. Wright, PhD, DSc, will receive the Homer W. Smith Award and deliver an address during Kidney Week. Dr. Wright will speak on "Renal Glucose Transport from Man to Molecule."

Dr. Wright is professor of physiology and Mellinkoff Professor in Medicine at the David Geffen School of Medicine at UCLA.

The Smith Award recognizes those who have made outstanding contributions to understanding how kidneys function in normal and diseased states, and Dr. Wright has been addressing these issues since before joining the faculty of the department of

As a student, Dr. Wright was fascinated by epithelial physiology and for his doctorate he studied the mechanism of active glucose transport across the intestine. He became interested in understanding active sodium glucose transporters (SGLTs) from the atomic level to their human physiology. He was the first to identify SGLT proteins, and his research team cloned the intestinal and renal transporter, SGLT1 and SGLT2. This discovery led to studies in which they identified mutations in the SGLT1 gene that cause glucose-galactose malabsorption. Dr. Wright has used biophysical and biochemical techniques to elucidate the atomic structure of an SGLT and the mechanisms of sodium glucose transport.

His recent interest is in how new diabetic drugs interact with SGLTs in the kidney and intestine. Working with his research partner, UCLA molecular and medical pharmacologist Jorge Barrio, PhD, Dr. Wright has used positron emission tomography to image SGLT activity throughout the body and to explore their functions in humans. The two are currently studying SGLT activity in human subjects and patients to parse out their role in health and disease.

Dr. Wright served as chair of the department of physiology at UCLA from 1987 to 2000. He has also been a visiting professor at the Center for Advanced Studies at the National Polytechnic Institute in Mexico, at the Max Planck Institute for Biophysics in Frankfurt, and at Queen Elizabeth College at the University of London.

He has published more than 300 peer-reviewed papers and reviews. He has trained some 45 students and fellows, many of whom now hold senior academic positions around the world. He is a fellow of the British Royal Society and a member of the German Academy of Sciences. His research has been supported continuously for 35 years by the National Institutes of Health.

Born in Northern Ireland, Dr. Wright received his doctorate in physiology from the University of Sheffield in the United Kingdom. He originally came to the United States for a fellowship in the biophysics laboratory at Harvard University.

## Homer W. Smith



Homer W. Smith was chairman of physiology at the University of Virginia before moving in 1928 to New York University (NYU). As director of the Physiology Laboratories at NYU, he developed and refined the concepts of glomerular filtration and tubular absorption and secretion of solutes.

The clarity of Dr. Smith's logic and the skill with which he explained his ideas transformed them into vivid and powerful concepts that are the cornerstones of our present understanding of normal and abnormal renal function. He attracted the best and brightest to the field, to NYU, and to the Mount Desert Island Biological Laboratory, where he spent many summers studying renal physiology in fish.

The Homer W. Smith award recognizes individuals who contribute to our basic understanding of how the kidneys function in health and disease.



## Expert on Rare Renal Disorder Tapped to Deliver Coburn Lectureship



Rajesh V. Thakker

tudies of unusual disorders can shed light on the working of the kidney, and the lessons from one of these disorders will be the subject of the Jack W. Coburn Endowed Lectureship on Friday, Nov. 2, at 2 p.m. "Stone Formation in Dent's Disease" will be the topic addressed by Rajesh V. Thakker, MD.

Dr. Thakker is the May Professor of Medicine at the University of Oxford. He was previously professor of medicine at the Royal Postgraduate Medical School, The Hammersmith Hospital, London, until 1999, when he took up his present position in Oxford.

Dent's disease is a renal tubular disorder

characterized by low-molecular-weight proteinuria, hypercalciuria, nephrolithiasis, nephrocalcinosis, and progressive renal failure. The disorder is caused by mutations in the X-chromosome-linked renal-specific chloride channel CLC-5. CLC-5 belongs to the family of voltage-gated chloride channels that function as homodimeric proteins.

Dent's disease has been reported in some 250 families. The main symptoms are generally found in males only, and may be present in early childhood. The care is supportive, focusing on the treatment of hypercalciuria and the prevention of kidney stones. Progression to end stage renal failure occurs between the third and fifth decades of life in 30 to 80 percent of affected males.

Dr. Thakker will discuss how molecular studies and the generation of mouse models of the disease have increased our understanding of the renal tubular mechanisms that regulate mineral homeostasis. The findings fit with his main research focus on the molecular basis of disorders of calcium homeostasis.

Dr. Thakker is currently chairman of the United Kingdom's National Institute for Health Research/Medical Research Council (MRC) Efficacy and Mechanisms Evaluations Board. He has served on the MRC Physiological Medicine and Infections Grants Committee (1994 to 1997), the MRC Clinical Training and Career Development Panel (1997 to 2000), the MRC Physiological Medicine and Infections Board (2000 to 2005), and the Council for the Society for Endocrinology (2003 to 2006). He served as secretary to the Forum on Academic Medicine for the Royal College of Physicians (United Kingdom) and the Academy of Medical Royal Colleges (2002 to 2005).

He has received many prizes, including the Young Investigator Award and the Louis V. Avioli Founder's Award from the American Society for Bone and Mineral Research, the Raymond-Horton Smith Prize (Cambridge University, United Kingdom), the Society for Endocrinology Medal (United Kingdom), the European Journal of Endocrinology Prize (European Federation of Endocrine Societies), and the Graham Bull Prize from the Royal College of Physicians (United Kingdom).

ASN gratefully acknowledges Amgen for support of the Jack W. Coburn Endowed Lectureship.

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## Authority to Address Allocation of Dialysis and Other Scarce Resources



Bruce C. Vladeck

it, academic, and business communities. He is a widely recognized expert in health care policy and finance.

Dr. Vladeck was administrator of the Health Care Financing Administration (HCFA, the predecessor of the Centers for Medicare & Medicaid Services) from 1993 through 1997, a period that included the Clinton administration's failed health care reform attempt, the Contract with America and switch to Republican control of Congress, budget stalemates, and the Balanced Budget Act of 1997.

the controversial issues involved in

the future allotment of health care resources will be the subject of the

Christopher R. Blagg Endowed Lectureship

in Renal Disease and Public Policy. An expert

with broad experience with Medicare and

other programs, Bruce C. Vladeck, PhD, will

speak on Friday, Nov. 2, at 2 p.m. on "Alloca-

Inc., a consulting subsidiary of the Greater

New York Hospital Association, which he

joined in 2009. His varied career has included

senior leadership roles in the public, nonprof-

Dr. Vladeck is a senior adviser to Nexera,

tion of Health Care: Dialysis and Beyond."

Dr. Vladeck's time at HCFA was marked by innovation in Medicaid programs through demonstration waivers, the development of Medicare prospective payment systems for many providers, and the implementation of the first quantitative quality measures for managed care plans. His work at HCFA was recognized in 1995 by a National Public Service Award. From 1998 to 1999 he served as a presidential appointee to the National Bipartisan Commission on the Future of Medicare.

After leaving HCFA, Dr. Vladeck spent 6 years as senior vice president for policy and as professor of health policy and geriatrics at Mount Sinai Medical Center in New York City. His assignments there ranged from managing the medical school's affiliation with New York's public hospital system to acting as interim chair of the department of geriatrics.

He served as interim president of the University of Medicine and Dentistry of New Jersey, which had lost its academic accreditation. During his 16-month tenure, he restored fiscal stability to the system; rebuilt its governance, compliance, and internal control processes; and laid the groundwork for restoration of its accreditation.

A graduate of Harvard College and the University of Michigan, Dr. Vladeck has held full-time faculty positions at Columbia University and Mount Sinai and has served as adjunct faculty at several institutions. He is a member of the Institute of Medicine and the New York Academy of Medicine and serves on the boards of the Medicare Rights Center, a nonprofit consumer service organization; Ascension Health; and the New York City Board of Health.

ASN gratefully acknowledges the Northwest Kidney Centers and its contributors for support of the Christopher R. Blagg Endowed Lectureship in Renal Disease and Public Policy.

## Dolph Chianchiano to Receive President's Medal



time and effective advocate for improving kidney care, Dolph Chianchiano, on Friday, Nov. 2. Mr.

**Dolph Chianchiano** 

Foundation (NKF) for 30 years, serving as senior vice president for health policy and research until his retirement in 2009. He continues to consult for the foundation as a health policy adviser.

Mr. Chianchiano spent 4 years in health-related research and policy work for the American Heart Association before joining the NKF in 1979 as an associate director, where he began crafting the initiatives that helped build the NKF.

He became the principal architect of NKF's public policy campaigns and author of NKF's position papers and policy statements. Under his leadership, NKF became a vigorous proponent of many legislative efforts, resulting in the passage of laws that have helped raise standards for dialysis facilities, expedited the transplantation process, removed barriers to organ donation, and provided funding for lifesaving treatments for kidney patients. As one example of his tenacity, it took 25 years of advocacy by the kidney community to convince the Food and Drug Administration to implement warning labels regarding the potential for kidney damage from over-the-counter nonsteroidal anti-inflammatory drugs in 2009.

Mr. Chianchiano was NKF's principal liaison with several coalitions and government agencies, including the Centers for Disease Control and Prevention, the National Institute of Diabetes and Digestive and Kidney Diseases, and the American Society of Transplant Surgeons.

As the administrator of NKF's research program, he made the important decision to expand the program to include not only grants to physicians, but to other members of the health-care team such as nurses, technicians, dietitians, and social workers. That program has distributed almost \$80 million in grants.

Mr. Chianchiano was the prime mover behind several of NKF's signature activities. He was the catalyst for the creation of three peer-reviewed medical journals, including the American Journal of Kidney Diseases. He helped develop the popular Spring Clinical Meetings in 1992. He spearheaded the initial Controversies in the Quality of Dialysis Care Conference, which led to the launch of the Kidney Disease Outcomes Quality Initiative, which has published 12 clinical practice guidelines and led to numerous advances in kidney treatment.

Former NKF chair John H. Kirkendall said of Mr. Chianchiano, "His vast knowledge, work ethic, and impeccable honesty are hallmarks everyone should strive for."

**\_EADING THE FIGHT AGAINST KIDNEY DISEASE** 



## ASN FOUNDATION FOR KIDNEY RESEARCH

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

# The Ben J. Lipps Research Fellowship Program

- Fund 10 new research applications and ten continuing projects a year beginning July 2013.
- Distribute \$50,000 a year per fellow for two years to conduct original, meritorious research.
- Announce Thursday, November 1, 2012, during the Opening Plenary Session of ASN Kidney Week 2012 in San Diego, CA.

## Funds 10 new research fellows annually, including:

- One Sharon Anderson Research Fellow (annually)
- Five Ben J. Lipps Research Fellows (annually)
- One George B. Rathmann Research Fellow (every other year)
- Three ASN Research Fellows (annually)

# 2013 FOUNDERS CIRCLE MEMBERS

## **Founders Circle**

The ASN Foundation Founders Circle recognizes donors year round for their generous contributions to the Ben J. Lipps Research Fellowship Program. Through this program, donors provide vital support to the next generation of physician scientists.

The ASN Foundation for Kidney Research gratefully acknowledges the following donors for their generous contributions.



## **Plenary Session**

## NIH Leader to Speak on Directions in Genomic Medicine



Eric D. Green

State-of-the-Art Lecture

The head of the National Human Genome Research Institute (NHGRI) will deliver a state-of-the-art lecture on "Entering the Era of Genomic Medicine: Research Opportunities and Challenges." Eric D. Green, MD, PhD, will speak on Saturday, Nov. 3.

As director of NHGRI at the National Institutes of Health (NIH) since 2009, Dr. Green is responsible for leading the investigative program and other initiatives of the largest organization in the world dedicated to genomics research.

He has been with the institute since 1994, previously serving as its scientific director (2002 to 2009), chief of its Genome Technology Branch (1996 to 2009), and director of the NIH Intramural Sequencing Center (1997 to 2009). While directing an independent research pro-

gram for almost two decades, Dr. Green was at the forefront of efforts to map, sequence, and understand eukaryotic genomes, including significant, startto-finish involvement in the Human Genome Project. This work blossomed into a productive program in comparative genomics that provided important insights about genome structure, function, and evolution.

Most recently, Dr. Green led NH-GRI's strategic planning process, which yielded a new vision for the future of genomics research, titled "Charting a Course for Genomic Medicine from Base Pairs to Bedside."

He is a founding editor of the journal *Genome Research* and a series editor of *Genome Analysis: A Laboratory Manual.* He is co-editor of *Annual Review of Genomics and Human Genetics.* He has authored or co-authored more than 280 scientific publications.

Prior to being recruited to join NIH in 1994, Dr. Green was assistant professor of pathology, genetics, and internal medicine and a co-investigator in the Human Genome Center at Washington University in St. Louis, the university where he received his medical degree and doctorate. For his doctorate in cell biology, Dr. Green studied sugar molecules attached to proteins. But when the Human Genome Project began to be discussed in the 1980s, he switched scientific fields to follow his clinical interests in molecular diagnostics.

Dr. Green has received many awards and honors, including the Helen Hay Whitney Postdoctoral Research Fellowship, a Lucille P. Markey Scholar Award in Biomedical Science, the Lillian M. Gilbreth Lectureship for Young Engineers at the National Academy of Engineering, an Alumni Achievement Award from the Washington University School of Medicine, and the Wallace H. Coulter Lectureship Award from the American Association for Clinical Chemistry.

## Donald Kohan to be Given Narins Award For Contributions in Education



Donald E. Kohan

onald E. Kohan, MD, PhD, FASN, who has been a leader in the educational efforts of ASN, will receive the Robert G. Narins Award for these and other contributions. Dr. Kohan is professor of medicine at the University of Utah Health Sciences Center in Salt Lake City.

He has served the University of Utah as chief of nephrology, nephrology fellowship training program director, and dean of graduate medical education. He has also been the chief of medicine at the Salt Lake City VA Medical Center.

The Narins Award honors those who have made substantial contributions to education

and teaching, and that has been the focus of Dr. Kohan's activities with ASN. He was the first ASN education director for nephrology fellowship training. He chaired the executive committee of the ASN training program directors (TPDs) from 2006 to 2011. He helped establish the subspecialty and ASN in-training examinations. He contributed to developing new Accreditation Council for Graduate Medical Education guidelines for nephrology, initiating development of nephrology fellowship curricula including geriatric nephrology, creating travel awards and programs for medical students at Kidney Week, developing learning experiences for residents at Kidney Week, creating Kidney Week pathways for educators including education-based abstracts and symposia, promoting awareness of nephrology workforce shortages, creating ASN nephrology TPD retreats, creating a course for new TPDs, redefining the structure of the TPD executive committee, and developing ASN webpages that contain extensive information for TPDs and nephrology fellows.

Dr. Kohan obtained a PhD in renal physiology in 1980 and an MD in 1982. For the past 25 years, his laboratory has examined the role of distal nephron autocoids, including endothelin, nitric oxide, prostaglandins, and other factors, in the control of urinary salt and water excretion and arterial pressure in health and in hypertension. His team pioneered renal cell-specific gene targeting.

Dr. Kohan has served on National Institutes of Health, VA, and American Heart Association study sections, including chairing the VA Nephrology Merit Review Committee. The importance of Dr. Kohan's research has been recognized by virtue of his election to the American Society of Clinical Investigation and the Association of American Physicians.

## Robert G. Narins



Robert G. Narins, MD, was the first recipient of the award now bearing his name. He taught and mentored countless students, serving on the faculties of the University of Pennsylvania, UCLA, Harvard University, Temple University, and Henry Ford Hospital. Well recognized for his contributions in the fields of fluid-electrolyte and acid-base physiology, Dr. Narins has also led numerous education efforts at the national

and international levels. Among these, he has chaired the American Board of Internal Medicine's Nephrology Board and worked on the American College of Physicians' Annual Program Committee. From 1994 to 2006, he developed and guided ASN's educational programs, including working to expand educational programs during Renal Week (Kidney Week). In addition, he was instrumental in the development of the Nephrology Self-Assessment Program (NephSAP and the *Clinical Journal of the American Society of Nephrology*; and in establishing the Fellow of the American Society of Nephrology program. Dr. Narins is also credited with working with organizations in Europe and Asia to help promote education and teaching in nephrology.

## Peters Award to Honor Thomas DuBose Jr.



SN will recognize the wide-ranging contributions of Thomas D. DuBose Jr., MD, FASN, MACP, with the presentation of the John P. Peters Award.

Dr. DuBose is the Tinsley R. Harrison Chair of Internal Medicine and professor of physiology and pharmacology at Wake Forest School of Medicine in Winston-Salem, NC. The 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, and Dr. Dubose's achievements span the field from research to service. Dr. DuBose has served as division chief of

Thomas D. DuBose Jr.

nephrology at two institutions, the University of Texas Medical Branch, Galveston, and the University of Texas Medical School, Houston. Prior to being recruited to Wake Forest, he was the Peter T. Bohan Professor and chair of the department of medicine at the University of Kansas School of Medicine.

Throughout his research career, Dr. DuBose has focused on elucidating factors governing the regulation of tubule transporters involved in urinary acidification and potassium homeostasis. These transporters have been implicated in monogenic diseases associated with renal tubular acidosis, the chronic metabolic acidosis of chronic progressive kidney disease, and abnormalities in potassium balance and blood pressure regulation.

His studies with Dr. David Good at the University of Texas uncovered the interdependence of potassium homeostasis and ammonium excretion. Their studies in animal models provided a better understanding of the role of hyperkalemia in the development of metabolic acidosis and of hypokalemia in the perpetuation of metabolic alkalosis, underscoring the importance of the correction of these conditions for treatment.

His studies using microelectrode methodology validated the reliability of the urine minus blood CO, tension as an index of distal tubule H+-secretion in the rat collecting duct, and extended these observations to experimental models of distal renal tubular acidosis. He and his colleagues were among the first to show that while both gastric and colonic  $\alpha$ -subunits of  $H^*$ ,  $K^*$ -ATPase play a role in urinary acidification in the kidney, the colonic  $\alpha$  H<sup>+</sup>,K<sup>+</sup>-ATPase is site-specifically upregulated in the collecting duct by potassium deprivation in an animal model of chronic hypokalemia. These studies showed the importance of this proton transporter in the metabolic alkalosis associated with hypokalemia.

Dr. DuBose is an author of 164 published papers and chapters in textbooks. With Dr. Lee Hamm he co-edited the text Acid-Base and Electrolyte Disorders.

Dr. DuBose served as ASN president in 2006. He has also served the society as chair of the Chronic Kidney Disease Advisory Group, a member of the board of advisors, and as its representative on the Council of Subspecialty Societies of the American College of Physicians. He chaired the American Heart Association Council on the Kidney in Cardiovascular Disease and served as a member of the board of regents of the American College of Physicians.

He has also received the Donald W. Seldin Award and the President's Award of the National Kidney Foundation, and the Distinguished Achievement Award of the American Heart Association Council on the Kidney in Cardiovascular Disease.

## John P. Peters



John P. Peters, MD, was one of the fathers of nephrology and former chief of the Metabolic Division in the Department of Medicine at Yale University. He transformed clinical chemistry from a discipline of qualitative impressions to one in which precise quantitative measurements of body fluids comprise a vital part of the patient examination and provide great explanatory value.

He advanced the view that disease is a quantitative abnormality of normal physiological processes and that, by understanding disease, one could gain a deeper understanding of normal physiology. His enduring scientific contributions paralleled his fervent mission to ensure that the physician be an advocate for the patient.

## ASN to Bestow Scribner Award on Nathan Levin

he Belding H. Scribner Award will be

tendered to Nathan W. Levin, MD,

FACP, FCP(SA), for his career-long

contributions to the practice of nephrology.

Dr. Levin is an attending physician at

Beth Israel Medical Center, a professor of

medicine at Mount Sinai School of Medicine

and Albert Einstein College of Medicine, and

chair of the Research Board of the Renal Research Institute, all in New York City.

His previous positions include being head

of the nephrology and hypertension division

at Henry Ford Hospital in Detroit and chief

of the renal section at the VA Research Hos-



Nathan W. Levin

pital in Chicago. He has been working in nephrology since 1957, when he immigrated to the United States from South Africa.

Established in 1995, the Scribner Award is presented to individuals who have made outstanding contributions to the care of patients with renal disorders or have substantially changed the clinical practice of nephrology.

Dr. Levin is the founder and past medical and research director of the Renal Research Institute (RRI), which under his leadership gained global recognition. RRI trains research fellows from countries around the world in kidney disease-related clinical research. Its research spans a full spectrum of interests from molecular biology, clinical research, and pharmaceutical trials to epidemiology.

Among his many activities to support the field, Dr. Levin co-chaired the National Kidney Foundation's Dialysis Outcomes Quality Initiative, where he made important contributions to the initiative's clinical practice guidelines. He is a member of the medical advisory board of the American Association of Kidney Patients, a founding member of the Sustainable Kidney Care Foundation, a member of the scientific advisory board of the Dialysis Outcomes and Practice Patterns Study, cochair of the dialysis advisory committee of the International Society of Nephrology (ISN), an executive committee member of the Kidney Disease: Improving Global Outcomes foundation, a co-founder of the South African Renal Society, and vice president of the Association for the Advancement of Medical Instrumentation.

He has also served as president of the Renal Physicians Association, president of New York Dialysis Services, chair of the Roche Foundation for Anemia Research, and a council member of ISN.

He has contributed to the dialysis and nephrology literature by authoring more than 350 peer-reviewed publications.

His many honors and awards include the Joel D. Kopple Award of the International Federation of Kidney Foundations, the Belding Scribner Trailblazer Award of the International Society for Hemodialysis, the Renal Physicians Association's Distinguished Nephrology Service Award, the Medal of Excellence of the American Association of Kidney Patients, the Fresenius Lifetime Achievement Award, the Association for the Advancement of Medical Instrumentation's Recognition Award, the National Kidney Foundation's Garabed Eknoyan Award, the Amgen Recognition Award, an American College of Physicians fellowship, and an honorary doctorate from the Medical University of Lublin, Poland.

## Belding H. Scribner



riovenous shunt, which made possible long-term hemodialysis for chronic renal failure.

of Washington's Division of Nephrology in the Department of Medicine from 1958 to 1982. He and his co-workers at the Seattle university made numerous contributions to helping patients with end stage renal disease, including establishing the world's first out-of-hospital di-

alysis unit, developing a home hemodialysis program, improving techniques and equipment for hemodialysis and peritoneal dialysis, and studying the adequacy and complications of chronic renal disease treated by dialysis. Dr. Scribner's work made a significant contribution to transforming nephrology into a major subspecialty of internal medicine.

Belding H. Scribner, MD, developed the arte-

Dr. Scribner served as head of the University

## **Plenary Session**

## **Trailblazer Explores** History and Outlook of **Kidney Disease**



Robert W. Schrier

cians.

"Where Kidney Disease Was and Where It Is Headed." Dr. Schrier chaired the department of med-

he past and fu-

ture of kidney

disease will be

the subject of a state-

of-the-art lecture on

Sunday, Nov. 4. Robert

W. Schrier, MD, pro-

fessor emeritus at the

University of Colorado,

Denver, will speak on

icine at the University of Colorado School of Medicine for 26 years and headed the division of renal diseases and hypertension for 20 years. In 1989, he was elected a member of the Institute of Medicine of the National Academy of Sciences. He has been president of the American Society of Nephrology, National Kidney Foundation, International Society of Nephrology, and Association of American Physi-

He has authored more than 1000 scientific papers and edited numerous books, including editions in internal medicine, geriatrics, drug usage, and kidney disease. His research contributions center on autosomal dominant polycystic kidney disease; pathogenesis of acute renal cell injury; hypertension and diabetic nephropathy; and renal and hormonal control of body fluid volume in cirrhosis, cardiac failure, nephrotic syndrome, and pregnancy. The National Institutes of Health has funded his research for more than 40 years.

During Dr. Schrier's tenure as chair of the department of medicine at the University of Colorado, the full-time faculty increased from about 75 to 500. The annual research grants the faculty received rose from \$3 million to \$100 million. As its staff and training programs became nationally prominent, the institution established 30 endowed research chairs. In recognition of these achievements, the governor of Colorado and mayor of Denver issued proclamations designating May 4, 2002, as Robert W. Schrier Day. That year, Dr. Schrier also received the prestigious Belle Bonfils-Stanton Award for Contributions in Science and Medicine.

Dr. Schrier has received honorary degrees from DePauw University, the University of Colorado, the University of Silesia, the University of Toledo, and the National Academy of Medicine of Belarus. He has received the highest awards of the American Society of Nephrology (John P. Peters Award), American College of Physicians (John Phillips Award), National Kidney Foundation (David Hume Award), International Society of Nephrology (Jean Hamburger Award), German Society of Nephrology (Franz Vollhard Award), Western Society of Clinical Investigation (Mayo Soley Award), Association of Professors of Medicine (Robert H. Williams Award), American Kidney Fund (National Torchbearer Award), Association of American Physicians (Francis Blake Award), Acute Renal Failure Commission (Bywaters Award), New York Academy of Medicine (Edward N. Gibbs Memorial Award), University of Strasburg (Louis Pasteur Medal), and American Association of Kidney Patients (Medal of Excellence). His international awards include the Grand Hamdan International Award for Medical Sciences (United Arab Emirates) and the Alexander von Humboldt Research Award (Germany).

## Young Investigator Attains **Recognition For Podocyte** Research



Tobias B. Huber

diseases of the kidney.

SN will present its Young Investigator Award to Tobias B. Huber, MD, for his groundbreaking research on podocyte biology. Dr. Huber will deliver the Young Investigator Address, titled "Podocyte Biology: The Key to Understanding Glomerular Diseases," on Sunday, Nov. 4.

Begun in 1985, and co-sponsored by the American Heart Association's Council of the Kidney, the Young Investigator Award recognizes an individual with an outstanding record of achievement and creativity in basic and patient-oriented research related to the functions and

Dr. Huber is an associate professor of medicine, principal investigator of the Speman Graduate School, and attending physician in the renal division at the Freiburg University Medical Center in Germany. His translational research program involves model organisms, transgenic mouse models, high-throughput screening, systems biology, and high-resolution imaging approaches to studying glomerular signaling pathways in health and disease. His team elucidated several key molecular mechanisms of podocyte biology and progressive glomerular disease. They identified signaling programs that regulate podocyte cell survival, endocytosis, cytoskeletal organization, and polarity, which provided novel insights into how podocytes contribute to glomerular diseases. Recently, Dr. Huber's team established a role of the mechanistic target of rapamycin (mTOR) gene and autophagy in progressive kidney disease and kidney aging. These studies have broad clinical implications, including for potential new therapeutic strategies. Dr. Huber received his doctoral and medical degrees and completed his nephrology fellowship at the University Medical Center in Freiburg. He conducted his postdoctoral work with Thomas Benzing and Gerd Walz in Freiburg, and Andrey Shaw at Washington University in St. Louis, where his observations led to the discovery of novel protein complexes and functions of the slit diaphragm. Dr. Huber has received numerous honors, including three from the German Society of Nephrology: the Young Nephrologist Award in 2002, the Hans U. Zollinger Research Award in 2009, and the Franz Volhard Award (the society's highest research award) in 2010.



LEADING THE FIGHT AGAINST KIDNEY DISEASE

# ASN Kidney Week 2012 EDUCATIONAL SYMPOSIA SCHEDULE

## Thursday, November 1 • 12:45 p.m. – 1:45 p.m.

Emerging Concepts in Pathophysiology and Treatment of Uremic Pruritus Support for this symposium is provided by an educational grant from Mitsubishi Tanabe Pharma

Membranous Nephropathy: Guidelines and Beyond Support for this symposium is provided by an educational grant from ROUESTCOR

 Support for this symposium is provided by an educational grant from



Balancing Phosphorus Control and Adherence in Maintenance Dialysis Patients Support for this symposium is provided by an educational grant from FRESENIUS MEDICAL CARE

## Friday, November 2 • 12:45 p.m. – 1:45 p.m.

Bundled Payments: Increased Transfusions, Changing Practice Patterns, No Quality Measures

This activity is supported by an educational donation provided by

Clinical Approach to Hyponatremia: The Nephrologist's Perspective Support for this symposium is provided by an educational grant from Otsuka Otsuka America Pharmaceutical, Inc.

It's All About Balance: How Calcium and Phosphorus Influence Management of CKD-MBD Support for this symposium is provided by an educational grant from SANOFI RENAL

**New Approaches to Anemia Management in Chronic Kidney Disease** Support for this symposium is provided by an educational grant from



## Saturday, November 3 • 6:45 a.m. - 7:45 a.m

Calcineurin Inhibitors in Kidney Transplantation: What Have We Learned? Where Do Things Stand?

Support for this symposium is provided by an educational grant from UNOVARTIS

**Innovation in a Bundled Payment Environment** 

This activity is supported by an educational donation provided by

## Saturday, November 3 • 12:45 p.m. – 1:45 p.m.

Advances in Pathogenesis and Treatment of Complement-Mediated Thrombotic Microangiopathies: aHUS and STEC-HUS

Support for this symposium is provided by an educational grant from KLEXION

Sponsored by ASN

**Basic Science Symposium: Nanomedicine and Nephrology** 

New Insights into the Management of Hyperparathyroidism in Dialysis and Kidney Transplant Patients

This activity is supported by an educational donation provided by

Thursday, November 1 – Saturday, November 3 San Diego Marriott Marquis and Marina

## **Continuing Education Credit**

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

Breakfast or lunch will be served at each session.

Seating is limited and available on a first-come, first-served basis to fully paid Annual Meeting participants.

Doors open 15 minutes prior to each session.





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ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE



As of 9/14/2012

## **Journal View**

## **Theophylline reduces** contrast medium nephropathy risk

The adenosine receptor antagonist theophylline may lower the risk of acute kidney injury (AKI) induced by radiocontrast medium, according to a meta-analysis in Kidney International.

A literature review identified 16 randomized controlled trials comparing adenosine antagonists with control treatments to prevent contrast medium-induced AKI. In both arms, treatment could be with or without N-acetylcysteine. Data on 1412 participants were pooled to compare contrast medium-induced AKI rates, change in serum creatinine, dialysis requirement, and in-hospital mortality.

On the basis of data from 13 trials (1412 patients), theophylline reduced the risk of contrast medium-induced AKI by about half: risk ratio 0.48. Theophylline also had a protective effect on absolute change in serum creatinine: standardized mean difference -0.31 mg/dL, based on 13 trials (1170 patients). It did not appear beneficial in patients with serum creatinine of 1.5 mg/dL or higher.

On metaregression analysis, the risk of contrast medium-induced AKI was related to baseline serum creatinine level. There was no consistent effect on rates of dialysis or in-hospital death, both of which were infrequent.

Animal studies have suggested that theophylline and aminophylline have the potential to protect kidney function after the injection of contrast medium. However, clinical studies of adenosine receptor antagonist treatment have yielded conflicting results.

Existing data suggest that theophylline reduces the risk of contrast medium-induced AKI, with a modest but significant improvement in kidney function after exposure to contrast medium. The authors call for high-quality randomized trials, including patients at different levels of baseline risk and evaluation of long-term outcomes [Bai B, et al. Effect of theophylline on prevention of contrast-induced acute kidney injury: a meta-analysis of randomized controlled trials. Am J Kidney Dis 2012; 60:360-370].

## Late episodes of acute rejection carry higher risk of graft loss

Acute rejection events become less frequent with time since transplantation, but later events may have a greater impact on graft survival, suggests a report in Transplantation.

The researchers analyzed U.S. Renal Data System data on 48,179 kidney transplantations from 2000 to 2007. The Organ Procurement and Transplant Network was used to gather data on acute rejection events, which were classified as antibody-treated or not. Acute rejection

was analyzed for association with all-cause graft loss, by use of a time-varying Cox regression approach.

The rate of non-antibody-treated acute rejection events (per 100 graft-years at risk) decreased from 9.93 6 months after transplantation to 8.43 at 12 months, 5.71 at 24 months, and 4.70 at 36 months. The rate of non-antibody-treated acute rejection was more than double the rate of antibody-treated events, across risk periods and donor types. Antibody-treated events were associated with a higher risk of graft loss than were non-antibody-treated events.

For antibody-treated acute rejection, the relative risk of graft loss increased with the time between transplantation and the rejection event. By contrast, the risk from non-antibody-treated events was highest 13 to 24 months after transplantation. Regardless of when acute rejection occurred, the associated risk of graft loss was higher in the first 89 days after the event, compared with 90 days and later.

This large study helps to clarify the rates and clinical impact of acute rejection after

## For renal transplant patients myfortic<sup>®</sup>: Consistent From Refill to Refill to Refill #1



Demonstrated efficacy and safety in de novo and maintenance renal transplant patients<sup>3-5</sup>

More than 81% of myfortic prescriptions<sup>1,‡</sup> had a \$0 co-pay with the Novartis Monthly Co-pay Card for eligible patients

Consistency also comes with savings: Start your new *myfortic* patients with a 30-day free trial<sup>§</sup> by visiting **www.myfortic.com** or by calling the Novartis Transplant Reimbursement Access Point at 1-877-952-1000.

MMF, mycophenolate mofetil. CELLCEPT is a registered trademark of Hoffmann-La Roche Inc.

\*As of January 13, 2012. <sup>†</sup>Based on data from the *myfortic* Co-pay Savings Program. Program is available to eligible patients taking *myfortic* and is subject to change without notice. *Not valid* for patients whose prescriptions are paid for by Medicare, Medicaid, or any other federally subsidized health care program, or for Massachusetts residents.

Initial prescription or refills based on 1-year transaction data (2011) for cash payment and insured patients combined. §Product coverage and program subject to change without notice

## Indication:

*myfortic*<sup>®</sup> (mycophenolic acid) delayed-release tablet is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

## Important Safety Information:

WARNING: EMBRYOFETAL TOXICITY, MALIGNANCIES, AND SERIOUS INFECTIONS

- Use during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations.
- Females of reproductive potential (FRP) must be counseled regarding pregnancy prevention and planning · Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma and other neoplasms. Only physicians experienced in immunosuppressive therapy and management of organ transplant recipients should prescribe myfortic® (mycophenolic acid) delayed-release tablet. Patients receiving myfortic should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient
- myfortic is contraindicated in patients with hypersensitivity to mycophenolate sodium, mycophenolic acid (MPA), mycophenolate mofetil (MMF), or to any of its excipients
- Embryofetal Toxicity: myfortic can cause fetal harm when administered to a pregnant female. Use of myfortic during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations

Please see additional Important Safety Information and Brief Summary of Prescribing Information, including Boxed WARNINGS, on adjacent pages.

kidney transplantation. Acute rejection occurring a longer time after transplantation may have a greater impact on the risk of graft loss, with risk being highest less than 90 days after the event [Lentine KL, et al. The implications of acute rejection for allograft survival in contemporary U.S. kidney transplantation. *Transplantation* 2012; 94:369–376].

## Peritransplantation NGAL and IL-18 predict 1-year graft function

Two biomarkers of kidney injury measured shortly after transplantation are associated with allograft function after 1 year, reports a study in the *Clinical Journal of the American Society of Nephrology*.

The prospective, multicenter study included 154 patients, mean age 54 years, undergoing deceased-donor kidney transplantation. The levels of neutrophil gelatinase–associated lipocalin (NGAL) and interleukin-18 (IL-18) were measured in early posttransplantation urine specimens. These biomarkers were evaluated for association with poor allograft function—defined

## Important Safety Information: (cont)

- Pregnancy Exposure Prevention and Planning: FRP must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations, and must be counseled regarding pregnancy prevention and planning. (See additional important Pregnancy Testing, Contraception, and Pregnancy Planning information below)
- Lymphoma and Other Malignancies: Patients receiving immunosuppressive regimens involving combinations of drugs, including *myfortic*, as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin
- Infections: Oversuppression of the immune system can also increase susceptibility to infection, fatal infections, and sepsis
- Polyomavirus Infections: Immunosuppressed patients are at increased risk for opportunistic infections, including Polyomavirus infections. Polyomavirus infections in transplant patients may have serious and sometimes fatal outcomes. These include cases of JC virus–associated progressive multifocal leukoencephalopathy (PML) and Polyomavirusassociated nephropathy (PVAN), especially due to BK virus infections, which have been observed in patients receiving *myfortic*. PVAN, especially due to BK virus infection, is associated with serious outcomes, including deteriorating renal function and renal graft loss. Patient monitoring may help detect patients at risk for PVAN
- Cases of PML have been reported in patients treated with MPA derivatives including MMF and mycophenolate sodium. PML, which is sometimes fatal, commonly presents with hemiparesis, apathy, confusion, cognitive deficiencies, and ataxia. Risk factors for PML include treatment with immunosuppressant therapies and impairment of immune function. In immunosuppressed patients, physicians should consider PML in the differential diagnosis in patients reporting neurological symptoms, and consultation with a neurologist should be considered as clinically indicated. Reduction in immunosuppression should be considered for patients who develop evidence of PML or PVAN. Physicians should also consider the risk that reduced immunosuppression represents to the graft
- Blood Dyscrasias Including Pure Red Cell Aplasia: Cases of pure red cell aplasia (PRCA) have been reported in patients treated with MPA in combination with other immunosuppressive agents. In some cases, PRCA was found to be reversible with dose reduction or cessation of therapy with MPA derivatives. In transplant patients, however, reduced immunosuppression may place the graft at risk. Patients receiving *myfortic* should be monitored for blood dyscrasias (eg, neutropenia or anemia). If blood dyscrasias occur (eg, neutropenia develops [ANC <1.3 x 10<sup>3</sup>/µL or anemia]), dosing with *myfortic* should be interrupted or the dose reduced, appropriate diagnostic tests performed, and the patient managed appropriately
- Pregnancy Testing: To prevent unplanned exposure during pregnancy, FRP should have a serum or urine pregnancy test
  with a sensitivity of at least 25 mIU/mL immediately before starting *myfortic*. Another pregnancy test with the same
  sensitivity should be done 8 to 10 days later. Repeat pregnancy tests should be performed during routine follow-up visits.
  Results of all pregnancy tests should be discussed with the patient. In the event of a positive pregnancy test, females
  should be counseled with regard to whether the maternal benefits of mycophenolate treatment may outweigh the risks to
  the fetus in certain situations
- Contraception: FRP taking myfortic must receive contraceptive counseling and use acceptable contraception during the entire myfortic therapy, and for 6 weeks after stopping myfortic, unless the patient chooses abstinence. Patients should be aware that myfortic reduces blood levels of the hormones in the oral contraceptive pill, and could theoretically reduce its effectiveness. (Please see package insert for acceptable contraceptive methods for females)
- Pregnancy Planning: For patients who are considering pregnancy, consider alternative immunosuppressants with less potential for embryofetal toxicity. Risks and benefits of *myfortic* should be discussed with the patient
- Gastrointestinal Disorders: Gastrointestinal bleeding (requiring hospitalization) has been reported in *de novo* renal transplant patients (1.0%) and maintenance patients (1.3%) treated with *myfortic* (up to 12 months)
- Patients with Renal Impairment: Subjects with severe chronic renal impairment (GFR <25 mL/min/1.73 m<sup>2</sup>) may present higher plasma MPA and MPAG AUC relative to subjects with lesser degrees of renal impairment or normal healthy volunteers. No data are available on the safety of long-term exposure to these levels of MPAG
- Concornitant Medications: Caution should be used with drugs that interfere with enterohepatic recirculation because of the
  potential to reduce efficacy
- Hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) Deficiency: myfortic should be avoided in patients with HGPRT deficiency such as Lesch-Nyhan and Kelley-Seegmiller syndrome
- Immunizations: Use of live attenuated vaccines should be avoided
- The principal adverse reactions associated with the administration of *myfortic* include constipation, nausea, and urinary tract infection in *de novo* patients and nausea, diarrhea, and nasopharyngitis in maintenance patients

References: 1. FDA approved drug products: mycophenolate mofetil. Drugs@FDA Web site. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search .Search\_drug\_name. Updated January 13, 2012. Accessed May 11, 2012. 2. Data on file. IMS Health, National Prescription Audit TRx Data: January 2011 to January 2012. 3. Salvadori M, Holzer H, de Mattos A, et al; on behalf of ERL B301 Study Groups. Enteric-coated mycophenolate sodium is therapeutically equivalent to mycophenolate mofetil in *de novo* renal transplant patients. *Am J Transplant.* 2004;4(2):231-236. 4. Myfortic<sup>®</sup> (mycophenolic acid\*) delayed-release tablets \*as mycophenolate sodium prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2012. 5. Budde K, Knoll G, Curtis J, et al; on behalf of ERL B302 Study Group. Long-term safety and efficacy after conversion of maintenance renal transplant recipients from mycophenolate mofetil (MMF) to enteric-coated mycophenolate sodium (EC-MPA, *myfortic<sup>®</sup>*). *Clin Nephrol.* 2006;66(2):103-111.

Please see Brief Summary of Prescribing Information, including **Boxed WARNINGS**, on adjacent pages.

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as an estimated GFR of less than 30 mL/ min/1.73 m<sup>2</sup>—at 1 year.

There was a 42 percent rate of delayed graft function. At 1 year, 16 percent of recipients met the study criteria for poor allograft function. Elevated levels of both biomarkers were significantly associated with the 1-year outcome. For patients with upper median values on the first day after transplantation, the adjusted odds ratios were 6.0 for NGAL and 5.5 for IL-18.

The net reclassification improvement was 36 percent for urine NGAL and 45 percent for IL-18. There was no significant interaction between the biomarkers and delayed graft function. Changes in biomarker levels over consecutive days showed a moderate trend with 1-year allograft function.

New approaches are needed to predict outcomes after kidney transplantation. This study suggests that elevated levels of urine NGAL and IL-18 are both associated with poor allograft function 1 year after transplantation. The biomarkers may have "potential for identifying patients for therapies that minimize the risk of additional injury," the investigators conclude [Hall IE, et al. Association between peritransplant kidney injury biomarkers and 1-year allograft outcomes. *Clin J Am Soc Nephrol* 2012; 7:1224–1233].

## Colonoscopy for screening after kidney transplantation?

Kidney transplant recipients have high rates of advanced colorectal neoplasia and cancers, which are better detected by colonoscopy than by fecal hemoglobin screening, suggests a study in the *British Medical Journal*.

The cross-sectional study included 229 Australian kidney transplant recipients, mean 9.0 years since transplantation. All were at least 50 years old and, aside from kidney transplantation, at average risk of colorectal cancer. The patients underwent fecal immunochemical testing for hemoglobin followed by colonoscopy with histologic examination of biopsy specimens. The two tests were compared for detection of advanced colorectal neoplasia: adenoma at least 10 mm in diameter, villous features, high-grade dysplasia, or colorectal cancer.

Advanced colorectal neoplasias were detected by colonoscopy in 13 percent of patients and by fecal hemoglobin in 12 percent. Colonoscopy detected colorectal cancer in five patients, three of whom had abnormal results on fecal hemoglobin testing.

The fecal test had 31 percent sensitivity and 90.5 percent specificity for the detection of advanced colorectal neoplasia; positive and negative predictive values were 32.1 percent and 90.1 percent, respectively. One additional case of advanced neoplasia would be detected for each eight colonoscopies performed.

## **Journal View**

## **Colonoscopy for** screening

## Continued from page 33

Colorectal cancer is a significant risk for long-term survivors of kidney transplantation. There are few data on colorectal screening for this group of patients; the current guidelines call for fecal hemoglobin screening in patients aged 50 or older.

The new study shows substantial rates of advanced colorectal neoplasia, including cancers, in patients with kidney transplants. Although fecal hemoglobin testing is "reasonably" specific, the sensitivity and positive predictive value are low. "[S]urveillance with colonoscopy may be the most appropriate approach to reduce the risk of colorectal cancer in kidney transplant recipients," the researchers write [Collins MG, et al. Screening for colorectal cancer and advanced colorectal neoplasia in kidney transplant recipients: cross-sectional prevalence and diagnostic accuracy study of faecal immunochemical testing for haemoglobin and colonoscopy. BMJ 2012; 345:e4657].

## **CKD** linked to increased stroke and embolism risk in AF

When chronic kidney disease (CKD) and atrial fibrillation (AF) occur together, the rates of stroke, thromboembolic events, and hemorrhage are higher than with AF alone, reports the New England Journal of Medicine.

Danish registries from 1997 to 2008 were used to identify 132,372 patients with nonvalvular atrial fibrillation. The risks of stroke, systemic thromboembolism, and bleeding were compared for patients with and without CKD. The risks and benefits of treatment with aspirin and warfarin were also compared.

Of this population of AF patients, 2.7 percent had non-end-stage CKD and 0.7 percent had end-stage disease requiring renal replacement therapy. The risks of stroke and systemic thromboembolism were elevated in both kidney disease groups: hazard ratio 1.49 for those with non-end-stage CKD and 1.83 for those receiving renal replacement therapy. The excess risks associated with kidney disease were lower for patients receiving warfarin, but not aspirin.

The bleeding risk was also increased for patients with kidney disease: hazard ratio 2.24 for non-end-stage CKD and 2.70 for disease requiring renal replacement therapy. These risks were further increased for patients taking warfarin, aspirin, or both. In the non-end-stage CKD group, higher doses of loop diuretics were associated with increased bleeding risk.

Atrial fibrillation and CKD are both associated with increased rates of stroke

or thromboembolism. The new study reports that both risks are significantly increased for patients with both diagnoses, compared with AF alone. Warfarin can lessen the risk of stroke or thromboembolism in patients with CKD and AF, but bleeding risk is increased with warfarin, aspirin, or both [Olesen JB, et al. Stroke and bleeding in atrial fibrillation with chronic kidney disease. N Engl J Med 2012; 367:625-635].

Kidney stones increase risk of later kidney disease A history of kidney stones carries a small but significant increase in the risk of loss of kidney function-ESRD-reports a study in the British Medical Journal.

Using the Alberta Kidney Disease Network database, the researchers identified more than 3 million adult patients who were free of ESRD or a history of pyelonephritis at baseline. Nearly 2 million had available data on outpatient serum creatinine levels. During follow-up, one or more kidney stones developed in about 27,000 patients—a rate of 0.8 percent. Kidney stones were evaluated as a risk factor for adverse renal outcomes, including incident ESRD, stage 3b to 5 chronic kidney disease (CKD), or sustained doubling of serum creatinine level.

The rates of adverse renal outcomes during follow-up were 0.2 percent for

#### **Mvfortic**® (mycophenolic acid\*) delayed-release tablets

\*as mycophenolate sodium Rx only

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

#### EMBRYOFETAL TOXICITY, MALIGNANCIES AND SERIOUS INFECTIONS

Use during pregnancy is associated with increased risks of first trimester pregnancy loss and congenital malformations. Females of reproductive potential (FRP) must be counsele regarding pregnancy prevention and planning. (see WARNINGS and PRECAUTIONS)

Immunosuppression may lead to increased susceptibility to infection and possible devel-opment of lymphoma and other neoplasms. Only physicians experienced in immunosup-pressive therapy and management of organ transplant recipients should use Myfortic<sup>®</sup> (mycophenolic acid). Patients receiving Myfortic should be managed in facilities equippe and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow up of the patient. (see WARNINGS and PRECAUTIONS) es equippe

INDICATIONS AND USAGE Myfortic® (mycophenolic acid) delayed-release tablets are indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

#### CONTRAINDICATIONS

Myfortic<sup>®</sup> (mycophenolic acid) is contraindicated in patients with a hypersensitivity to mycophenolate sodium, mycophenolic acid, mycophenolate mofetil, or to any of its excipients.

MARNINGS (SEE BOXED WARNING) EMBRYOFETAL TOXICITY Myfortic can cause fetal harm when administered to a pregnant female. Use of Myfortic during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increase risk of congenital malformations, especially external ear and other facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney (see **PRECAUTIONS: Prennarcy)**. PRECAUTIONS: Pregnancy).

Pregnancy Exposure Prevention and Planning Females of reproductive potential must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy pre-vention and planning. For recommended pregnancy testing and contraception methods (see PRECAUTIONS: Pregnancy Exposure Prevention and Planning).

Lymphoma and Other Malignancies Patients receiving immunosuppressive regimens involving combinations of drugs, including Mytoritic<sup>®</sup> (mycophenolic acid), as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin (see ADVERSE REACTIONS) The risk appears to be related to the intensity and duration of immunosuppression rather than to the upper developing lymphomas and the malignameters and the terms of the upper developing lymphomas and the malignancies, particularly of the skin (see ADVERSE REACTIONS) The risk appears to be related to the intensity and duration of immunosuppression rather than to the upper developing the state of the st the use of any specific agent.

The rates for lymphoproliferative disease or lymphoma in Myfortic-treated patients were compa-rable to the mycophenolate mofetil group in the *de novo* and maintenance studies (see ADVERSE **REACTIONS**). As usual for patients with increased risk for skin cancer, exposure to sunlight and UV light should be limited by wearing protective clothing and using a sunscreen with a high pro-tection factor.

#### Infections

Oversuppression of the immune system can also increase susceptibility to infection, including opportunistic infections, fatal infections, and sepsis. Fatal infections can occur in patients receiving immunosuppressive therapy (see ADVERSE REACTIONS).

## Polyomavirus Infections

ruyumavirus Intections Patients receiving immunosuppressants, including Myfortic are at increased risk for opportun infections, including Polyomavirus infections. Polyomavirus infections in transplant patients m have serious, and sometimes, fatal outcomes. These include cases of JC virus associated pro-gressive multifocal leukoencephalopathy (PML) and Polyomavirus associated nephropathy (PVAN) especially due to BK virus infection which have been observed in patients receiving Myfortic.

PVAN, especially due to BK virus infection, is associated with serious outcomes, in orating renal function and renal graft loss (see ADVERSE REACTIONS). Patient mo help detect patients at risk for PVAN.

Cases of PML, have been reported in patients treated with MPA derivatives which include mycophenolate mofetil (MMF) and mycophenolate sodium (see ADVERSE REACTIONS). PML, which is sometimes fatal, commonly presents with hemiparesis, apathy, confusion, cognitive deficiencies and ataxia. Risk factors for PML include treatment with immunosuppressant thera-pies and impairment of immune function. In immunosuppressed patients, physicians should consider PML in the differential diagnosis in patients reporting neurological symptoms and con-sultation with a neurologist should be considered as clinically indicated.

Reduction in immunosuppression should be considered for patients who develop evidence of PML or PVAN. Physicians should also consider the risk that reduced immunosuppression repre sents to the functioning allograft.

Blood Dyscrasias including Pure Red Cell Aplasia Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolic acid (MPA) derivatives in combination with other immunosuppressive agents. The mechanism for MPA derivatives induced PRCA is unknown; the relative contribution of other immunosuppres-sants and their combinations in an immunosuppressive regimen is also unknown. In some cases sams and their combinations in an immunosuppressive regimen is also unknown. In some cases PRCA was found to be reversible with dose reduction or cessation of therapy with MPA deriva-tives. In transplant patients, however, reduced immunosuppression may place the graft at risk. Changes to Myfortic therapy should only be undertaken under appropriate supervision in trans-plant recipients in order to minimize the risk of graft rejection (see ADVERSE REACTIONS, Post-marketing Experience).

Patients receiving Myfortic should be monitored for blood dyscrasias (e.g. neutropenia or and Patients receiving Myfortic should be monitored for blood dyscrasias (e.g. neutropenia or anemia (see PRECAUTIONS, Laboratory Tests). The development of neutropenia may be related to Myfortic itself, concomitant medications, viral infections, or some combination of these events. If blood dyscrasias occur (e.g. neutropenia (ANC <1.3x10<sup>2</sup>/ µL or anemia)), dosing with Myfortic should be interrupted or the dose reduced, appropriate diagnostic tests performed, and the patient man-aged appropriately (see DOSAGE AND ADMINISTRATION in the full prescribing information). Patients receiving Myfortic should be instructed to immediately report any evidence of infection, unexpected bruising, bleeding, or any other manifestation of bone marrow suppression.

Concomitant Use Myfortic has been administered in combination with the following agents in clinical trials antithymocyte/lymphocyte immunoglobulin, muromonab-CD3, basiliximab, datizumab, cyclo-sporine, and corticosteroids. The efficacy and safety of Myfortic in combination with other immunosuppression agents have not been determined.

#### PRECAUTIONS

Pregnancy Exposure Prevention and Planning Females of reproductive potential must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy p pregnancy loss and co vention and planning. ICV Dre-

Females of reproductive potential include girls who have entered puberty and all women who have a uterus and have not passed through menopause. Menopause is the permanent end of menstruation and fertility. Menopause should be clinically confirmed by a patient's healthcare practitioner. Some commonly used diagnostic criteria include 1) 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy) or 2) post-surgical from a bilateral oophorectomy.

Pregnancy Testing To prevent unplanned exposure during pregnancy, females of reproductive potential should have a serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL immediately before start-ing Mytoritic. Another pregnancy test with the same sensitivity should be done 8 to 10 days later. Repeat pregnancy tests should be performed during routine follow-up visits. Results of all preg-nancy tests should be discussed with the patient.

In the event of a positive pregnancy test, females should be counseled with regard to whether the maternal benefits of mycophenolate treatment may outweigh the risks to the fetus in certain situations.

#### Contraceptio

Females of reproductive potential taking Myfortic must receive contraceptive counseling and use acceptable contraception (see Table 4 for Acceptable Contraception Methods). Patients must use acceptable birth control during entire Myfortic therapy, and for 6 weeks after stopping Myfortic, unless the patient chooses abstinence (she chooses to avoid heterosexual intercourse completebil).

ceptive pill and could theoretically reduce its effectiveness (see PRECAUTIONS: Information for Patients and PRECAUTIONS: Drug Interactions: Oral Contraceptives). Table 4. Accentable Contractions: The Contraceptive set of the Contraceptive set of

## Table 4 Acceptable Contraception Methods for Females of Reproductive Potential

## Pick from the following birth control options:

Patient's partner had a vasectomy R Option 2 boom 6 Methods boom 6	Choose One Hormone Method AND One Barrier Method	Estrogen and Progesterone Oral Contraceptive Pill Transdermal patch Vaginal ring Progesterone-only Injection	AND	Diaphragm with spermicide Cervical cap with spermicide Contraceptive sponge Male condom Female condom	
Patient's partner had a vasectomy	Ontion 2	Hormone Methods		Barrier Methods	
Intrauterine devices (IUDs)	Methods to Use Alone	Intrauterine devices (IUDs) Tubal sterilization Patient's partner had a vasectomy			

Option 3	Barrier Methods choose 1		Barrier Methods choose 1
Choose One Barrier Method from each column <i>(must choose two methods)</i>	Diaphragm with spermicide Cervical cap with spermicide Contraceptive sponge	AND	Male condom Female condom

**Pregnancy Planning** For patients who are considering pregnancy, consider alternative immunosuppressants with less potential for embryofetal toxicity. Risks and benefits of Myfortic should be discussed with the

## patient.

patient. **Gastrointestinal Disorders** Gastrointestinal bleeding (requiring hospitalization) has been reported in *de novo* renal transplant patients (1.0%) and maintenance patients (1.3%) treated with Myfortic<sup>®</sup> (mycophenolic acid) (up to 12 months). Intestinal perforations, gastrointestinal hemorrhage, gastric ulcers and duodenal ulcers have rarely been observed. Most patients receiving Myfortic were also receiving other drugs known to be associated with these complications. Patients with active peptic ulcer disease were excluded from enrollment in studies with Myfortic. Because MPA derivatives have been associated with an increased incidence of digestive system adverse events, including infrequent cases of gastrointestinal tract ulceration, hemorrhage, and perforation, Myfortic should be admin-istered with caution in patients with active serious digestive system disease (**see ADVERSE REACTIONS**).

Patients with Renal Impairment Subjects with severe chronic renal impairment (GFR <25 mL/min/1.73 m<sup>2</sup>) may present higher plasma MPA and MPAG AUGs relative to subjects with lesser degrees of renal impairment or nor-mal relative volunteers. No data are available on the safety of long-term exposure to these levels

In the *de novo* study, 18.3% of Myfortic patients versus 16.7% in the mycophenolate mofetil group experienced delayed graft function (DGF). Although patients with DGF experienced a higher incidence of certain adverse events (anemia, leukopenia, and hyperkalemia) than patients without DGF, these events in DGF patients were not more frequent in patients receiving Myfortic com-pared to mycophenolate mofetil. No dose adjustment is recommended for these patients; how-ever, such patients should be carefully observed (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION in the full prescribing information).

**Concomitant Medications** In view of the significant reduction in the AUC of MPA by cholestyramine when administered with mycophenolate mofetil, caution should be used in the concomitant administration of Myfortic with drugs that interfere with enterohepatic recirculation because of the potential to reduce the efficacy (see PRECAUTIONS, Drug Interactions).

ESRD, 4.0 percent for stage 3b to 5 CKD, and 3.0 percent for doubling of serum creatinine. Compared with stonefree patients, those with even one episode of kidney stones were at increased risk of all three outcomes: adjusted hazard ratio 2.16 for ESRD, 1.74 for CKD, and 1.94 for doubling of serum creatinine.

The excess risk related to kidney stones appeared greater for women and for people younger than 50, although the

association was significant for both sexes and all age groups. Absolute increases in risk were small: the unadjusted ESRD rate was 2.48 per million person-days in those with kidney stones versus 0.52 per million in those without stones.

Kidney stones are a common and potentially preventable problem. There are few data on their possible association with later kidney disease.

This population-based study finds

significant increases in the risk of ESRD and other adverse renal outcomes in patients with even a single episode of kidney stones. Absolute increases in risk are small. More research is needed to understand the mechanism of the associations and the best way to prevent kidney stones, particularly in young women [Alexander RT, el al. Kidney stones and kidney function loss: a cohort study. BMJ 2012; 345:e5287].

## Low graft function linked to increased mortality



Among kidney transplant recipients in stable condition, lower levels of kidney function are independently associated with mortality risk, according to a report in the American Journal of Transplantation.

The authors performed a post hoc analysis of a trial evaluating the effects of homocysteine-reducing B vitamins after kidney transplantation. The analysis included 4016 patients, mean age 52 years, 20 percent with a history of cardiovascular disease (CVD). Estimated GFR (eGFR) was evaluated for associations with incident CVD and all-cause mortality, adjusted for demographic factors, clinical and transplant characteristics, and traditional CVD risk factors.

Complete data were available for 3676 patients, who had 527 CVD events over a median follow-up time of 3.8 years. In the adjusted model, below a cutoff point of 45 mL/min/1.73 m<sup>2</sup>, higher eGFR levels were associated with reduced risks of CVD and death. For both outcomes, the hazard ratio was 0.85 for each 5 mL/  $\,$ min/1.73 m<sup>2</sup> increase in eGFR. No association was present at eGFR levels of 45 mL/min/1.73 m<sup>2</sup> or higher.

Although CVD is the main cause of mortality after kidney transplantation, it has been unclear how kidney function affects posttransplantation CVD outcomes. This study finds that below 45 mL/min/1.73 m<sup>2</sup>, higher eGFR levels are independently associated with a lower incidence of CVD and a lower risk of death. "[R]educed kidney function itself rather than preexisting comorbidity may lead to CVD," the researchers conclude [Weiner DE, et al. Kidney function and risk of cardiovascular disease and mortality in kidney transplant recipients: the FAVORIT trial. Am J Transpl 2012; 12:2437–2445].

Myfortic® (mycophenolic acid\*) delayed-release tablets \*as mycophenolate sodium

**Patients with HGPRT Deficiency** On theoretical grounds, because Myfortic is an IMPDH Inhibitor, it should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome.

Immunizations During treatment with Myfortic, the use of live attenuated vaccines should be avoided and ts should be advised that vaccinations may be less effective (see PRECAUTIONS, Drug patients should be advised that Interactions, Live Vaccines).

#### Laboratory Tests

**Laboratory lests** Complete blood count should be performed weekly during the first month, twice monthly for the second and the third month of treatment, then monthly through the first year. If neutropenia develops (ANC <1.3×10<sup>3</sup>/µL), dosing with Myfortic should be interrupted or the dose reduced, appropriate tests performed, and the patient managed accordingly (see WARNINGS).

## Drug Interactions

ng drug interaction studies have been conducted with Myfortic Gastroprotective agents

**Castroprotective agems** Antacids with magnesium and aluminum hydroxides: Absorption of a single dose of Myfortic was decreased when administered to 12 stable renal transplant patients also taking magnesium-aluminum-containing antacids (30 mL): the mean  $C_{max}$ and AUQ<sub>(b+1)</sub> values for MPA were 25% and 37% lower, respectively, than when Myfortic was administered alone under fasting conditions. It is recommended that Myfortic and antacids not be administered simultaneously.

r a study conducted in 12 healthy volunteers, the pharmacokinetics of MPA were observed to be similar when a single dose of 720 mg Myfortic was administered alone and following concomi-tant administration of Myfortic and pantoprazole, which was administered at a dose of 40 mg BID tant admin for 4 days.

## **Cyclosporine:** When studied in stable renal transplant patients, cyclosporine, USP (MODIFIED) pharmacokinetics were unaffected by steady-state dosing of Myfortic.

The following recommendations are derived from drug interaction studies conducted following the administration of mycophenolate mofetil:

Acyclovir/Ganciclovir: May be taken with Myfortic; however, during the period of treatment, physicians should monitor blood cell counts. Both acyclovir/ganciclovir and MPAG concentral are increased in the presence of renal impairment, their coexistence may compete for tubular secretion and further increase in the concentrations of the two.

Azathioprine/Mycophenolate Moletil: Given that azathioprine and mycophenolate mofetil inhibit purine metabolism, it is recommended that Myfortic not be administered concomitantly with aza thioprine or mycophenolate mofetil.

Cholestyramine and Drugs that Bind Bile Acids: These drugs interrupt enterohepatic recircul tion and reduce MPA exposure when coadministered with mycophenolate mofetil. Therefore, or not administer Myfortic with cholestyramine or other agents that may interfere with enterohep recirculation or drugs that may bind bile acids, for example bile acid sequestrates or oral acti-vated charcoal, because of the potential to reduce the efficacy of Myfortic. cophenolate mofetil. Therefore, do

**Oral Contraceptives:** In a drug-drug interaction study, mean levonorgesterol AUC was decreased by 15% when coadministered with mycophenolate moteril. Although Myfortic may not have any influence on the ovulation-suppressing action of oral contraceptives, it is recommended to co-administer Myfortic with hormonal contraceptives, (e.g. birth control pill, transdermal patch, vaginal ring, injection, and implant) with caution and additional barrier contraceptive methods must be used. (see PRECAUTIONS: Pregnancy Exposure Prevention and Planning).

Live Vaccines: During treatment with Myfortic, the use of live attenuated vaccines should be avoided and patients should be advised that vaccinations may be less effective. Influenza vaccina-tion may be of value. Prescribers should refer to national guidelines for influenza vaccination (see PRECAUTIONS. General).

Drugs that after the gastrointestinal flora may interact with Myfortic by disrupting enterohepatic recirculation. Interference of MPAG hydrolysis may lead to less MPA available for absorption.

Carcinogenesis, Mutagenesis, Impairment of Fertility In a 104-week oral carcinogenicity study in rats, mycophenolate sodium was not tumorigenic at daily doses up to 9 mg/kg, the highest dose tested. This dose resulted in approximately 0.6-1.2 times the systemic exposure (based upon plasma AUC) observed in renal transplant patients at the recommended dose of 1.44 g/day. Similar results were observed in a parallel study in rats gm-formed with mycophenolate mofetii. In a 104-week oral carcinogenicity study in mice, mycopheno-late mofetil was not tumorigenic at a daily dose level as high as 180 mg/kg (which corresponds to 0.6 times the proposed mycophenolate sodium therapeutic dose based upon body surface area).

0.6 times the proposed infocuptendiate solution therapedic close based upon body striked rear. The genotoxic potential of mycophenolate sodium was determined in five assays. Mycophenolate sodium was genotoxic in the mouse lymphoma/thymidine kinase assay, the micronucleus test in V79 Chinese hamster cells, and the *in-vivo* mouse micronucleus assay. Mycophenolate sodium with the bacterial mutation assay (Salmonella typhimurium TA 1535, 97a, 98, 100, & 102) or the chromosomal aberration assay in human lymphocytes. Mycophenolate mofetil generated similar genotoxic activity. The genotoxic activity of MPA is probably due to the depletion of the nucleotide synthesis as a result of the pharmacodynamic mode of action of MPA (inhibition of nucleotide synthesis).

Mycophenolate sodium had no effect on male rat fertility at daily oral doses as high as 18 mg/kc and exhibited no testicular or spermatogenic effects at daily oral doses of 20 mg/kg for 13 weeks (approximately two-fold the therapeutic systemic exposure of MPA). No effects on female fertility were seen up to a daily dose of 20 mg/kg, which was approximately three-fold higher than the rec-ommended therapeutic dose based upon systemic exposure.

Pregnancy Pregnancy Category D (See WARNINGS) Following oral or IV administration, MMF is metabolized to mycophenolic acid (MPA), the active ingredient in Myfortic and the active form of the drug. Use of MMF during pregnancy is associ-ated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations, especially external ear and other facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney. In animal studies, con-genital malformations and pregnancy loss occurred when pregnant rats and rabbits received mycophenolic acid at dose multiples similar to and less than clinical doses. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Risks and benefits of Myfortic should be discussed with the patient. When appropriate, consider alternative immunosuppressants with less potential for embryofetal toxicity. In certain situations, the patient and her healthcare practitioner may decide that the maternal benefits outweigh the risks to the fetus. For those females using Myfortic at any time during pregnancy and those becoming pregnant within 6 weeks of discontinuing therapy, the healthcare practitioner should report the pregnancy to the Mycophenolate Pregnancy Registry (1-800-617-8191). The health-care practitioner should strongly encourage the patient to enroll in the pregnancy registry. The information provided to the registry will help the Health Care Community to better understand the effects of mycophenolate in pregnancy.

effects of mycophenolate in pregnancy. In the National Transplantation Pregnancy Registry (NTPR), there were data on 33 MMF-exposed pregnancies in 24 transplant patients; there were 15 spontaneous abortions (45%) and 18 live-born infants. Four of these 18 infants had structural malformations (22%). In postmarketing data (collected from 1995 to 2007) on 77 women exposed to systemic MMF during pregnancy, 25 had spontaneous abortions and 14 had a malformed infant or fetus. Six of 14 malformed offspring had ear abnormalities. Because these postmarketing data are reported voluntarily, it is not always possible to reliably estimate the frequency of particular adverse outcomes. These malformations are similar to findings in animal reproductive toxicology studies. For comparison, the background rate for congenital anomalies in the United States is about 3%, and NTPR data show a rate of 4-5% among babies born to organ transplant patients using other immunosuppressive drugs. There are no relevant qualitative or quantitative differences in the teratogenic potential of mycophenolate sodium and mycophenolate mofetil. mycophenolate sodium and mycophenolate mofetil.

In a teratology study performed with mycophenolate sodium in rats, at a dose as low as 1 mg/ malformations in the offspring were observed, including anophthalmia, exencephaly and umbil hernia. The systemic exposure at this dose represents 0.05 times the clinical exposure at the dose of 1.44 g/day Myfortic. In teratology studies in rabbits, fetal resorptions and malformation occurred from 80 mg/kg/day, in the absence of maternal toxicity (dose levels are equivalent to about 0.8 times the recommended clinical dose, corrected for BSA).

Nursing Mothers It is not known whether MPA is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from MPA, a decision should be made whether to discontinue the drug or to discontinue nursing while on treatment or within 6 weeks after stopping therapy, tak-ing into account the importance of the drug to the mother.

Pediatric Use De novo Renal Transplant The safety and effectiveness of Myfortic in *de novo* pediatric renal transplant patients have not been established.

#### Stable Renal Transplant

Stable Renal Transplant There are no pharmacokinetic data available for pediatric patients <5 years. The safety and effec-tiveness of Myfortic have been established in the age group 5-16 years in stable pediatric renal transplant patients. Use of Myfortic in this age group is supported by evidence from adequate and well-controlled studies of Myfortic in stable adult renal transplant patients. Limited pharmaco-kinetic data are available for stable pediatric renal transplant patients. Limited pharmaco-kinetic data are available for stable pediatric renal transplant patients in the age group 5-16 years. Pediatric doses for patients with BSA <1.19 m<sup>2</sup> cannot be accurately administered using currently available formulations of Myfortic tables (see CLINICAL PHARMACOLOGY, Special Populations and DOSAGE AND ADMINISTRATION in the full prescribing information).

Genative Use Patients ≥65 years may generally be at increased risk of adverse drug reactions due to immuno-suppression. Clinical studies of Myfortic did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other durations. drug therapy.

#### ADVERSE REACTIONS

ADVENSE REACTIONS The incidence of adverse events for Myfortic<sup>®</sup> (mycophenolic acid) was determined in random ized, comparative, active-controlled, double-blind, double-dummy trials in prevention of acute rejection in *de novo* and maintenance kidney transplant patients.

The principal adverse reactions associated with the administration of Myfortic include consti-pation, nausea, and urinary tract infection in *de novo* patients and nausea, diarrhea and nasopharyngitis in maintenance patients.

Adverse events reported in  $\geq 20\%$  of patients. Adverse events reported in  $\geq 20\%$  of patients receiving Myfortic or mycophenolate mofetil in the 12-month *de novo* renal study and maintenance renal study, when used in combination with cyclosporine, USP (MODIFIED) and corticosteroids, are listed in Table 5. Adverse event rates were similar between Myfortic and mycophenolate mofetil in both *de novo* and maintenance

#### Table 5 Adverse Events (%) in Controlled de novo and Maintenance Renal Studies

	de novo	de novo Renal Study		ice Renal Study
	Myfortic <sup>®</sup>	mycophenolate mofetil	Myfortic <sup>®</sup>	mycophenolate mofetil
	1.44 g/day (n=213)	2 g/day (n=210)	1.44 g/day (n=159)	2 g/day (n=163)
Blood and Lymphatic Syst	em Disorders			
Anemia	21.6	21.9	-	-
Leukopenia	19.2	20.5	-	-
Gastrointestinal System D	lisorders			
Constipation	38.0	39.5	-	-
Nausea	29.1	27.1	24.5	19.0
Diarrhea	23.5	24.8	21.4	24.5
Vomiting	23.0	20.0	-	-
Dyspepsia	22.5	19.0	-	-
Infections and Infestation	S			
Urinary Tract Infection	29.1	33.3	-	-
CMV Infection	20.2	18.1	-	-
Nervous System Disorder				
Insomnia	23.5	23.8	-	-
Surgical and Medical Pro	cedure			
Postoperative Pain	23.9	18.6	-	-

Geriatric Use

## **Journal View**

## Higher anion gap linked to increased mortality

A higher serum anion gap early in the course of kidney disease is associated with significantly increased mortality, reports a study in Kidney International.

Using data on 11,957 adults from the National Health and Nutrition Examination Survey 1999 to 2004, the researchers analyzed the relation between the anion gap, as a marker of kidney function, and mortality. Laboratory data were used to calculate the anion gap by the traditional method, with adjustment for albumin, or the full anion gap reflecting other electrolytes. The frequency of elevated anion gap relative to GFR was analyzed, including its association with mortality risk in study participants without advanced kidney disease.

The "traditional" anion gap was elevated only in participants with estimated GFR less than 45 mL/min/1.73 m<sup>2</sup>. By contrast, significant elevations were found for the albumin-adjusted

anion gap in patients with GFR values less than 60 mL/min/1.73  $m^2$ , and for the full anion gap at GFR values of 90  $mL/min/1.73 m^2$ .

With adjustment for body mass index, comorbidities, and other covariates, higher anion gap levels were associated with increased mortality. For the highest versus lowest quartiles, the relative hazard ratios were 1.62 for the albumin-adjusted anion gap and 1.64 for the full anion gap.

Uremia is associated with an increased serum anion gap, but it has been unclear whether elevations can occur earlier in the course of kidney disease. This study presents evidence that higher anion gaps can also occur with less advanced kidney disease and are associated with increased mortality. The authors call for further studies "to identify the unmeasured anions and to determine their physiological significance." [Abramowitz MK, et al. The serum anion gap is altered in early kidney disease and associates with mortality. Kidney Int 2012; 82:701-709].

#### Myfortic® (mycophenolic acid\*) delayed-release tablets \*as mycophenolate sodium

Table 6 summarizes the incidence of opportunistic infections in *de novo* and maintenance trans-plant patients, which were similar in both treatment groups.

	de novo	Renal Study	Maintenar	e Renal Study	
	wytortic®	mycopnenolate mofetil	wytortic®	mycopnenolate	
	1.44 g/day (n = 213)	2 g/day (n = 210)	1.44 g/day (n = 159)	2 g/day (n = 163)	
	(%)	(%)	(%)	(%)	
Any Cytomegalovirus	21.6	20.5	1.9	1.8	
- Cytomegalovirus Disease	4.7	4.3	0	0.6	
Herpes Simplex	8.0	6.2	1.3	2.5	
Herpes Zoster	4.7	3.8	1.9	3.1	
Any Fungal Infection	10.8	11.9	2.5	1.8	
- Candida NOS	5.6	6.2	0	1.8	
- Candida Albicans	2.3	3.8	0.6	0	

The following opportunistic infections occurred rarely in the above controlled trials: aspergillus and cryptococcus.

The incidence of malignancies and lymphoma is consistent with that reported in the literature for this patient population. Lymphoma developed in 2 *de novo* patients (0.9%), (one diagnosed 9 days after treatment initiation) and in 2 maintenance patients (1.3%) (one was AIDS-related), receiving Myfortic with other immunosuppressive agents in the 12-month controlled clinical trials. Nonmelanoma skin carcinoma occurred in 0.9% *de novo* and 0.6% maintenance patients.

The following adverse events were reported between 3% to <20% incidence in *de novo* and main-tenance patients treated with Myfortic in combination with cyclosporine and corticosteroids are tenance patients listed in Table 7.

## Table 7 Adverse Events Reported in 3% to <20% of Patients Treated with Myfortic<sup>®</sup> in Combination with Cyclosporine\* and Corticosteroids

	de novo Renal Study	Maintenance Renal Study
Blood and Lymphatic Disorders	Lymphocele, thrombocytopenia	Leukopenia, anemia
Cardiac Disorder	Tachycardia	
Eye Disorder	Vision blurred	-
Endocrine Disorders	Cushingoid, hirsutism	-
Gastrointestinal Disorders	Abdominal pain upper, flatulence, abdominal distension, sore throat, abdominal pain lower, abdominal pain, gingival hyperplasia, loose stool	Vomiting, dyspepsia, abdominal pain, constipation, gastroesophageal reflux disease, loose stool, flatulence, abdominal pain upper
General Disorders and Administration Site Conditions	Edema, edema lower limb, pyrexia, pain, fatigue, edema peripheral, chest pain	Fatigue, pyrexia, edema, chest pain, peripheral edema
Infections and Infestations	Nasopharyngitis, herpes simplex, upper respiratory tract infection, oral candidiasis, herpes zoster, sinusitis, wound infection, implant infection, pneumonia	Nasopharyngitis, upper respiratory tract infection, urinary tract infection, influenza, sinusitis
Injury, Poisoning, and Procedural Complications	Drug toxicity	Postprocedural pain
Investigations	Blood creatinine increased hemoglobin decrease, blood pressure increased, liver function tests abnormal	Blood creatinine increase, weight increase
Metabolism and Nutrition Disorders	Hypocalcemia, hyperuricemia, hypophosphatemia, hypochosphatemia, hypercholesterolemia, hyperkalemia, hypomagnesemia, diabetes mellitus, hyperphosphatemia, dehydration, fluid overload, hyperglycemia, hypercalcemia	Dehydration, hypokalemia, hypercholesterolemia
Musculoskeletal and Connective Tissue Disorders	Back pain, arthralgia, pain in limb, muscle cramps, myalgia	Arthralgia, pain in limb, back pain, muscle cramps, peripheral swelling, myalgia
Nervous System Disorders	Tremor, headache, dizziness (excluding vertigo)	Headache, dizziness
Psychiatric Disorders	Anxiety	Insomnia, depression
Renal and Urinary Disorders	Renal tubular necrosis, renal impairment, dysuria, hematuria, hydronephrosis, bladder spasm, urinary retention	-
Respiratory, Thoracic and Mediastinal Disorders	Cough, dyspnea, dyspnea exertional	Cough, dyspnea, pharyngolaryngeal pain, sinus congestion
Skin and Subcutaneous Tissue Disorders	Acne, pruritus	Rash, contusion
Surgical and Medical Procedures	Complications of transplant surgery, postoperative complications, postoperative wound complication	_
Vascular Disorders	Hypertension, hypertension aggravated, hypotension	Hypertension
*USP (MODIFIED)		

The following additional adverse reactions have been associated with the exposure to MPA when administered as a sodium salt or as mofetil ester

Gastrointestinal: Colitis (sometimes caused by CMV), pancreatitis, esophagitis, intestinal perfo-ration, gastrointestinal hemorrhage, gastric ulcers, duodenal ulcers, and ileus (see PRECAUTIONS) Resistance Mechanism Disorders: Serious life-threatening infections such as meningitis and nections endocarditis have been reported occasionally and there is evidence of a higher fre-quency of certain types of serious infections such as tuberculosis and atypical mycobacterial infectious en infection

**Respiratory:** Interstitial lung disorders, including fatal pulmonary fibrosis, have been reported rarely with MPA administration and should be considered in the differential diagnosis of pulmonary symptoms ranging from dyspnea to respiratory failure in posttransplant patients receiving MPA derivatives.

Postmarketing Experience: The following adverse reactions have been identified during post-approval use of Myfortic. Because these reactions are reported voluntarily from a population of uncertain size, reliably estimating their frequency or establishing a causal relationship to drug exposure is not always possible. Congenital disorder: Embryofetal toxicity: Congenital malformations and an increased incidence rted following exposure to mycophenolate mofetil of first trimester pregnancy loss have been reported followi (MMF) during pregnancy (see PRECAUTIONS: **Pregnancy**).

Infections: Cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal, have been reported in patients treated with MPA derivatives (see WARNINGS, Polyomavirus Infec-tions). Polyomavirus associated nephropathy (PVAN), especially due to BK virus infection, has been observed in patients receiving immunosuppressants, including Myfortic. This infection is associated with serious outcomes, including deteriorating renal function and renal graft loss (see WARNINGS, Polyomavirus Infections). WARNINGS, Polyomavirus Infections).

Hematologic: Cases of pure red cell aplasia (PRCA) have been reported in patients treat: MPA derivatives in combination with other immunosuppressive agents (see WARNINGS) Dermatologic: Cases of rash have been reported in patients treated with MPA derivatives

#### OVERDOSAGE

Signs and Symptoms

There has been no reported experience of acute overdose of Myfortic® (mycophenolic acid) in humans.

Possible signs and symptoms of acute overdose could include the following: hematological abnor-malities such as leukopenia and neutropenia, and gastrointestinal symptoms such as abdominal pain, diarrhea, nausea and vomiting, and dyspepsia.

#### Treatment and Management

Treatment and Management General supportive measures and symptomatic treatment should be followed in all cases of over-dosage. Although dialysis may be used to remove the inactive metabolite MPAG, it would not be expected to remove clinically significant amounts of the active moiety MPA due to the 98% plasma protein binding of MPA. By interfering with enterohepatic circulation of MPA, activated charcoal or bile acid sequestrants, such as cholestyramine, may reduce the systemic MPA exposure.

Storage Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Protect from moisture. Dispense in a tight container (USP).

Handling Tablets should not be crushed or cut. **Manufactured by:** Novartis Pharma Stein AG Stein, Switzerland Distributed by: Novartis Pharmaceuticals Corporation East Hanover, New Jersey 07936

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T2012-126 June 2012

## **Rising rate of dialysis** after major surgery

In Ontario, the use of short-term dialysis after elective major surgery has increased sharply since the mid-1990s, reports a study in the Canadian Medical Association Journal.

Using Ontario health databases, the researchers analyzed more than 550,000 adults undergoing elective major surgery between 1995 and 2009. Trends in the rate of short-term dialysis (within 14 days) after surgery were analyzed, along with the outcomes of death within 90 days and the need for long-term dialysis.

The analysis included 2231 patients receiving short-term dialysis—overall rate 0.4 percent. However, the rate of short-term dialysis increased steadily: from 0.2 percent in 1995 to 0.6 percent in 2009. Patients undergoing cardiac and vascular surgery accounted for most of the increase. After cardiac surgery, the rate of short-term dialysis increased from 1 in 390 patients to 1 in 85 patients. The trend remained significant after adjustment for patient and surgical characteristics: odds ratio 1.7.

The 90-day mortality in patients receiving short-term dialysis was 42.0 percent, with no change over time. Of 1294 patients who received short-term dialysis and survived, 27.2 percent received dialysis.

The rates of short-term dialysis after surgery appear to be increasing. It is particularly important to understand the trends and outcomes of short-term dialysis associated with elective surgical procedures.

This study documents a substantial increase in the use of short-term dialysis after elective major cardiac and vascular surgery. The associated rates of death and long-term dialysis are stable and high. The results highlight the need for better approaches to the prevention and treatment of acute perioperative kidney injury [Siddiqui NF, et al. Secular trends in acute dialysis after elective major surgery-1995 to 2009. CMAJ 2012; 184:1237–1245].

## **Bundled Payment Report** Finds Inconsistent Effects on Quality of Care

## By Kurtis Pivert

new review reports the use of bundled payments resulted in reduced health expenditures and small, but inconsistent, effects on patient care measures. The Agency for Healthcare Research and Quality (AHRQ) study did not evaluate the Medicare ESRD Prospective Payment System (PPS) and largely examined non-nephrology care. Researchers also examined how different designs for bundling services (e.g., payment methodology or risk-adjustment methods) and varying contextual factors (e.g., market variables or patient characteristics) influenced these outcomes. With health care spending continuing to rise and the report's conclusion that bundled payments may reduce costs, AHRQ's review should be assessed in the context of how the current dialysis bundled payment system influences care for patients with kidney disease.

The review Bundled Payment: Effects on Health Care (1) is part of a new AHRQ series -Closing the Quality Gap: Revisiting the State of the Science-that "aims to provide critical analysis of the existing literature on quality improvement strategies for a selection of diseases and practices." Bundled payments were evaluated because of "weak but consistent evidence" that these systems maintained the quality of health care while reducing associated costs. Researchers performed a literature review and selected 58 studies assessing the effects of bundled payments on health care spending and quality published between 1985 and 2011. Most studies were observational and in total examined 20 different implementations of bundled payments, including a Japanese study on bundling of hemodialysis medications.

Using bundled payments, physicians can apportion patient care in an effective manner, which "should create a financial incentive for providers to reduce the number and cost of services contained in the bundle," according to the AHRQ review. Although researchers found evidence of this, the average reduction in expenditures after changing from a fee-for-service model to bundled payments was 10 percent or less, while the decrease in health care utilization ranged from 5 to 15 percent.

The effects on patient care were generally small but less uniform, with several studies on similar bundled payment systems reporting worse, similar, or improved quality measures after the change was introduced. A lack of both standardized outcome metrics and homogenous data contributed to this finding. Also missing was evidence on the negative consequences of bundled payments, although some studies did report a decrease in health care utilization through the transfer of patients to other care settings.

The diversity of bundling systems in the report precluded researchers from examining the impact of different designs and contextual factors. Also, the studies included focused on single institutional providers and were complete prior to recent implementations of PPSs (such as the Medicare ESRD PPS), which limited the generalizability of the findings. Despite observing consistent reductions in health care spending, AHRQ concluded "the strength of the body of evidence was rated as low," and the results may not reflect the performance of current or future bundled payment models.

## **Bundled payments and nephrology**

The AHRQ review included a Japanese study (2) on bundling payments for anemia medications for patients on hemodialysis. Investigators following 3206 patients during the 1-year bundled payment rollout period found no change in the proportion of patients receiving recombinant human erythropoietin but an 11.8 percent reduction in dosage and a 9.6 percent increase in intravenous iron prescriptions. Patient care was assessed with hemoglobin levels, which remained stable during implementation of the bundling system.

Rajnish Mehrotra, MD, FASN-professor of medicine in the division of nephrology at the University of Washington and section chief at Harborview Medical Center in Seattle-recently co-authored a CJASN article (3) comparing mandated health care reforms, including the ESRD PPS and Quality Improvement Program (QIP), accountable care organizations, and the Affordable Care Act. He too has noted "evidence of reductions in use of erythropoietis-stimulating agents (ESAs) and increase in use of iron," in the United States after the introduction of the ESRD PPS, which "could be deemed as a 'reduction in healthcare utilization." He notes "if you take the quality measure and goal of reducing patients treated with ESAs with hemoglobin levels >12 g/dL, there has been a profound reduction in use, approximately a 10 percent absolute decrease. On the other hand, there have been some increases in the number of transfusions, which is a potentially adverse effect."

The AHRQ report stated that quality incentives were not "an intrinsic part of the bundled payment mechanism," in many of the systems evaluated, even though the risk for negative effects exists. These include "underuse of effective services within the bundle, avoidance of high-risk patients, and an increase in the number of bundles reimbursed," the authors said. Ensuring a basic level of quality of care was a factor behind the ESRD Quality Improvement Program (QIP), the first mandated pay for performance initiative.





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The American Society of Nephrology congratulates the 2012 ASN Research Fellowship Recipients and their meritorious research projects.

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Yale University School of Medicine Utilizing novel biomarkers and discovery proteomics for the differential diagnosis of acute kidney injury in patients with cirrhosis

## Lisa Boyette, MD, PhD

University of Pittsburgh School of Medicine Monocyte subsets in human renal transplantation

## Peter Czarnecki, MD

Harvard Medical School—Beth Israel Deaconess Medical Center Cellular functions of the cystic kidney disease protein Nek8 in ciliary protein homeostasis

## **David Drew, MD**

Tufts University School of Medicine FGF-23, ADMA and cognitive impairment in hemodialysis patients

## Heon Yung Gee, MD, PhD

University of Michigan Medical School Functional characterization of the novel FSGS-causing genes ARHGDIA and MED28

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## Julie Ishida, MD

University of California, San Francisco, School of Medicine Influence of intravenous iron on infection risk in hemodialysis patients

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Yale University School of Medicine The crosstalk of HGF and Wnt signaling in kidney repair

#### Ciaran McMullan, MD

Harvard Medical School-Brigham and Women's Hospital Association of blood pressure variability on incidence and progression of chronic kidney disease

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## **Bundled Payment**

Continued from page 37

Current quality measures for ESRD lack a strong evidence base, and Mehrotra said "there is a compelling need to identify additional metrics and determine whether they provide better information on patient risk and health, such as efficiency and patient centeredness of care." Comparative effectiveness research into how health care practices affect outcomes is needed because "there's virtually no data on whether implementing the bundle improves any of these other measures," he said.

The utilization of current metrics to assess performance in the QIP poses a threat to the individualization of patient care, Mehrotra said. "One size does not fit all, and this is particularly true with the management of a complex disease like ESRD." An example he points to is the proposed mineral metabolism measure, which will penalize facilities with a higher proportion of patients with calcium levels >10.2 mg/ dL. "Yet the data that identifies calcium of 10.2 mg/dL as 'dangerous' or 'bad' is very weak, and a clinical trial that randomizes patients to different calcium levels is needed to determine whether it affects outcomes." Just as the AHRQ review concluded, Mehrotra expects the use of bundled payments to expand, saying that "the perverse incentive of rewarding volume of care has to diminish, otherwise it is difficult to see how health care costs will come down." But he sees benefits in the current dialysis bundle in "the rapid growth of the home dialysis population, which I personally believe to be a good development and is in line with the goals of CMS."

#### References

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## **Industry Spotlight**

## Kidney cancer roundup

Pfizer Inc. says that its oral drug Inlyta (axitinib) has been granted European approval for use as a second-line therapy for kidney cancer patients, according to Reuters News. The drug, already approved in the United States, has been approved in Europe as a second-line treatment for patients who have not responded to initial chemotherapy.

The company announced that the approval was based on data from a clinical trial showing that the drug significantly extended progression-free survival in patients who did not respond to treatment with a different Pfizer drug, Sutent.

In January 2012, axitinib was approved in the United States for the same indication as the European approval. Axitinib works by inhibiting proteins that can influence tumor growth and cancer progression.

Renal cell carcinoma (RCC) affects 102,000 people in Europe every year, the company reported.

In other kidney cancer news, Seattle Genetics has embarked on a clinical trial to assess the safety of its monoclonal antibody-based therapy for advanced kidney cancer. The phase 1b trial will also measure the compound's ability to fight the tumors safely. The compound, called SGN-75, is taken in combination with a cancer drug called everolimus to treat kidney cancer. Everolimus is an oral prescription medication used to treat advanced RCC when certain other medicines, such as sunitinib or sorafenib, have not worked.

SGN-75 is an antibody-drug conjugate composed of an antibody attached to a synthetic cell-killing agent, using Seattle Genetics' proprietary technology, according to the website *Investor Report*.

"We are encouraged by the preliminary single-agent activity and tolerability demonstrated by SGN-75 in RCC patients and by our preclinical data suggesting synergy," with drugs like everolimus, called mTOR inhibitors, said Jonathan Drachman, MD, senior vice president of research and translational medicine at Seattle Genetics. He said that his company looks forward to learning whether the combination "can provide therapeutic benefit to patients who currently have limited treatment options."

According to Seattle Genetics, the study is expected to enroll up to 40 patients at several centers in the United States and is enrolling patients who have previously been treated with one or two tyrosine kinase inhibitor drugs. For the fourth consecutive year since a federal data registry program was launched in 2007, Fresenius' chronic kidney disease data registry has been the largest registry for nephrology. Fresenius and dozens of other registries have gained admittance as official registries in the federal program that requires physician quality-indicator reporting. That program, the Physicians Quality Reporting System (PQRS) is administered by the Centers for Medicare and Medicaid Services (CMS).

The Fresenius registry, known as Acumen PQRS, has been a qualified CMS data registry since 2009. In 2015, participation will be required of all eligible medical professionals who are eligible to report the work as described by the required indicators. The PQRS federal program was designed to enhance the quality of information reported by health care professionals.

"Acumen PQRS will continue to provide nephrologists with the best data registry for their practices," said Terry Ketchersid, MD, vice president and medical officer for Fresenius Medical Care, who directs the Acumen registry. "We are committed to maintaining our level of excellence."

The program uses both financial incentives and penalties to ensure high-quality reporting. The system pays physicians incentive bonuses for appropriate and correct use of registry reporting of quality measures. Beginning in 2015, eligible professionals who don't participate will face a payment adjustment.

Fresenius still largest nephrology quality data registry

The Acumen database added 700 new reporting members last year, Fresenius reported.

Each year, the measures can change in content. The Renal Physicians Association (RPA) has taken an active role in developing the nephrology measures used by the program. On September 4, the group wrote to Marilyn Tavenner, acting administrator for CMS, and asked for consideration of the same suggested quality measures submitted to CMS nearly a year ago, in October 2011. An example of a suggested quality measure would be percentage of calendar months within a 12-month period during which patients 18 years old and older with a diagnosis of ESRD who were receiving hemodialysis or peritoneal dialysis had a hemoglobin level below 10 g/dL.

The American Medical Association notes that "the CMS believes these quality initiatives aim to empower providers and consumers with information that would support the overall delivery and coordination of care, and ultimately would support new payment systems that provide more financial resources to provide improved quality care." Currently CMS reimburses for the volume of covered services.

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Today, Mitsubishi Tanabe Pharma is dedicated to bringing new treatments for renal disease and other conditions to the U.S. through our U.S. subsidiary.



