ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

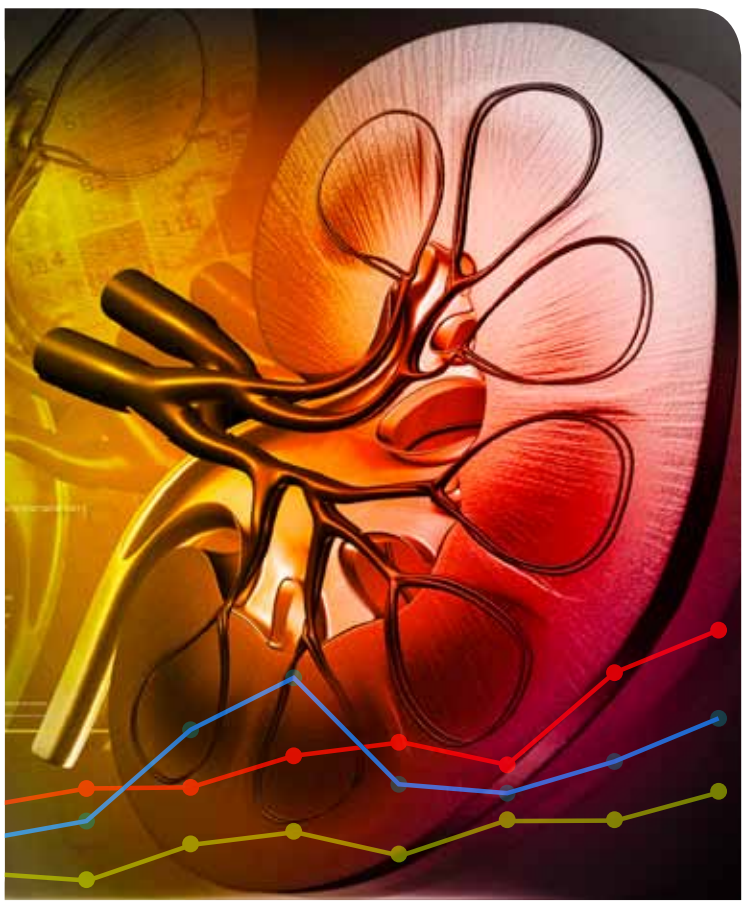
KIDNEY WEEK EDITION

Kidney News

October/November 2014 | Vol. 6, Numbers 10 & 11

Federal Report to Assess Adequacy of Investment in Kidney Research

By Grant Olan



U.S. Congressional Kidney Caucus Co-Chair Rep. Tom Marino (R-PA) recently requested a Government Accountability Office (GAO) report to review the state of federal investments in kidney research. Obtaining a congressional request for a GAO report on this topic is the cornerstone of ASN's aggressive new Research Advocacy Strategic Plan to bolster support for more federal kidney research funding.

In addition to assessing the adequacy of investments in kidney research compared to the cost of kidney care, Rep. Marino asked the GAO to identify areas of kidney disease knowledge gaps, as well as recent scientific advances that are most likely to improve patient outcomes and reduce care costs for people on dialysis.

"As a kidney cancer survivor, I care deeply about the millions of Americans affected with kidney disease—including the more than 16,000 Pennsylvanians on dialysis—and want to ensure they receive the best possible care. This is possible only through smart, adequate investments in the most promising areas of research," Rep. Marino said.

An ASN analysis revealed that total federal investments in kidney research are less than 1 percent of what Medicare spends on the cost of care for the more than 20 million Americans with a chronic kidney disease diagnosis (approximately $650 million for kidney research vs. $80 billion in Medicare expenditures). The analysis also revealed that kidney disease ranks near the bottom of the list of research investments per patient by the National Institutes of Health—the largest funder of medical research in the world.

"Considering the significant public health burden to patients, families, and Medicare, a GAO report will help the kidney care and scientific community better understand where investments in research can make the biggest gains for our patients and the American public," ASN President Sharon M. Moe, MD, FASN, said. "Rep. Marino's support in requesting the report is a prime example of his longstanding commitment to the kidney community and is one of the many, many reasons I am proud to present him with the 2014 ASN President's Medal. Together with his Kidney Caucus co-chair, Rep. Jim McDermott (D-WA), who is also receiving the 2014 ASN President's Medal, Rep. Marino is a tremendous advocate, and I commend his leadership."

Kidney Care Partners (KCP), a broad coalition of dialysis providers, patient groups, and health professional organizations dedicated to advancing patient care, supported ASN's goal of obtaining the report and also backed a provision in a comprehensive kidney care bill directing the GAO to commission the report.

"KCP supports research that improves pa-

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KIDNEY WEEK SCIENTIFIC SESSIONS

THURSDAY

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Young Investigator Award: Myles Wolf

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Our Roots Go Deep

Kidney Research Investments

Continued from page 1

tient care and outcomes. Kidney disease afflicts millions of people, and I suspect the GAO report will conclude what the kidney community already suspects, that kidney research is underfunded," said KCP Chairman Edward R. Jones, MD. "I want to recognize ASN in particular for its advocacy on behalf of the report, and to especially thank Rep. Marino for submitting the request."

NIH research funding by disease

Disease (Prevalence in millions)*	**2013 budget**	**NIH spending per patient**
HIV/AIDS (1.1)†	$2,898,000,000	$2,635
Cancer (14.5)††	$7,477,000,000	$516
Alzheimer's (5.2)§	$504,000,000	$98
Heart Disease (26.6)†	$1,634,000,000	$61
Diabetes (29.1)‖	$1,007,000,000	$34
Kidney Disease (20)†	$591,000,000	$30

Sources: *National Institutes of Health, † Centers for Disease Control and Prevention, ††American Cancer Society, §Alzheimer's Association, ‖ American Diabetes Association

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KidneyNews

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ASN Kidney Week—New in 2014

This year's Kidney Week includes exciting new features and resources.

Early Programs

ASN offers 13 Early Programs on Tuesday, November 11, and/or Wednesday, November 12, preceding the Annual Meeting (November 13–16). The new Early Programs are:

- **Advances in Research Conference—Building a Kidney: From Stem Cells to Function** focuses on exploring concepts, innovations, and best practices in tissue regeneration as it relates to the kidney.
- **Coming to a Unit Near You: Cluster-Randomized Trials in Hemodialysis** addresses this novel approach to evidence development that is particularly well-suited for the hemodialysis setting.
- **Human Genetics in Nephrology: Clinical Fundamentals and Research Advances** provides an introduction to key topics in human genetics and genomics, followed by in-depth discussions of the full gamut of genetic diseases and syndromes.
- **Innovation in Kidney Disease, Dialysis, and Vascular Access** describes novel approaches to the treatment of kidney disease by focusing on techniques, devices, and scientific methods in various stages of development.
- **Nephro-Pharmacology across the Spectrum of Kidney Diseases** is a comprehensive review of fundamental issues related to clinical pharmacology in kidney disease. Participants should note that Continuing Pharmacy Education credits are available for this program.

Michelle P. Winn, MD, Endowed Lectureship

This lectureship honors Dr. Michelle Winn's wide-ranging achievements in glomerular disease and genetics, as well as her many contributions to increasing opportunities in medicine and research. ASN is pleased to award the inaugural Michelle P. Winn Endowed Lectureship to Dr. Andrey S. Shaw, who will present a lecture on "Genetics of Human FSGS" on Friday, November 14, at 2:00 p.m.

ASN gratefully acknowledges Duke University School of Medicine, the school's Division of Nephrology, and several individuals for support of this lectureship.

Streamlined Onsite Program

This year, the Kidney Week Onsite Program contains poster sessions but not individual abstract titles and authors. For abstract titles, authors, and more, please refer to the Kidney Week Mobile App, the "Locate Me" Kiosks for Posters and Exhibits in the exposition halls, or the Abstract Supplement PDF available at www.asn-online.org/KidneyWeek.

Certificates of Attendance

For Early Programs, international participants may pick up printed Certificates of Attendance (not CME certificates for U.S. participants) on Wednesday, November 12, at their individual program.

For the Annual Meeting, international participants may access online Certificates of Attendance (not CME certificates for U.S. participants) from November 14, 2014, through February 13, 2015, at https://www.showreg.net/ASN1411S/CERT. Certificates are only available if you have picked up your meeting materials or printed your meeting badge onsite. If you have questions, please visit the ASN Service Center in the Grand Hall of the Pennsylvania Convention Center.

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*Based on a mean of 8.4 ± 4.4 PB pills per day[1]

INDICATION:
Phoslyra is a phosphate binder indicated for the reduction of serum phosphorus in patients with end stage renal disease (ESRD). Phoslyra is administered orally with food.

IMPORTANT SAFETY INFORMATION:

- **Phoslyra is contraindicated in patients with hypercalcemia.**
- **Patients should have serum calcium levels closely monitored and their dose of Phoslyra adjusted or terminated to bring levels to normal.** No other calcium supplements should be given concurrently with Phoslyra.
- Phoslyra may decrease the bioavailability of tetracyclines or fluoroquinolones.
- There are no empirical data on avoiding drug interactions between calcium acetate or Phoslyra and most concomitant drugs. When administering an oral medication with Phoslyra where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, administer the drug 1 hour before or 3 hours after Phoslyra or calcium acetate. Monitor blood levels of the concomitant drugs that have a narrow therapeutic range.
- The most common (>10%) adverse reactions experienced with Phoslyra are hypercalcemia, nausea, and diarrhea. Of the observed drug-related adverse reactions, diarrhea (5/38, 13.2%) was more common with Phoslyra than with a solid formulation calcium acetate.
- Phoslyra may cause diarrhea with nutritional supplements that contain maltitol.

For additional important safety information, please see the brief Prescribing Information on this page.

Reference: 1. Sussman E, Mullon C, Ginsberg N, et al. Amount of fluid ingested with phosphate binders in hemodialysis-dependent CKD patients. Poster and abstract presented at National Kidney Foundation 2010 Spring Clinical Meeting, April 15-17, 2010, Orlando, Fla.

Manufactured for and distributed by: Fresenius Medical Care NA, Waltham, MA 02451. For more information on Phoslyra, please contact Fresenius Medical Care NA at 800-323-5188.

PN 102352-01 Rev. A 04/2014

Brief Summary: Consult full package insert for complete Prescribing Information.

INDICATIONS AND USAGE: Phoslyra® (calcium acetate oral solution 667 mg per 5 mL) is a phosphate binder indicated to reduce serum phosphorus in patients with end stage renal disease (ESRD). Management of elevated serum phosphorus levels usually includes all of the following: reduction in dietary intake of phosphate, removal of phosphate by dialysis, and inhibition of intestinal phosphate absorption with phosphate binders.

DOSAGE AND ADMINISTRATION: The recommended initial dose of Phoslyra for the adult dialysis patient is 10 mL with each meal. Increase the dose gradually to lower serum phosphorus levels to the target range, as long as hypercalcemia does not develop. Titrate the dose every 2 to 3 weeks until an acceptable serum phosphorus level is reached. Most patients require 15–20 mL with each meal.

CONTRAINDICATIONS: Patients with hypercalcemia.

WARNINGS AND PRECAUTIONS:

Hypercalcemia. Patients with end stage renal disease may develop hypercalcemia when treated with calcium, including calcium acetate (Phoslyra). Avoid the concurrent use of calcium supplements, including calcium-based nonprescription antacids, with Phoslyra. An overdose of Phoslyra may lead to progressive hypercalcemia, which may require emergency measures. Therefore, early in the treatment phase during the dosage adjustment period, monitor serum calcium levels twice weekly. Should hypercalcemia develop, reduce the Phoslyra dosage or discontinue the treatment, depending on the severity of hypercalcemia. More severe hypercalcemia (Ca >12 mg/dL) is associated with confusion, delirium, stupor and coma. Severe hypercalcemia can be treated by acute hemodialysis and discontinuing Phoslyra therapy. Mild hypercalcemia (10.5 to 11.9 mg/dL) may be asymptomatic or manifest as constipation, anorexia, nausea, and vomiting. Mild hypercalcemia is usually controlled by reducing the Phoslyra dose or temporarily discontinuing therapy. Decreasing or discontinuing Vitamin D therapy is recommended as well. Chronic hypercalcemia may lead to vascular calcification and other soft-tissue calcification. Radiographic evaluation of suspected anatomical regions may be helpful in early detection of soft tissue calcification. The long-term effect of Phoslyra on the progression of vascular or soft tissue calcification has not been determined.

Hypercalcemia (>11 mg/dL) was reported in 16% of patients in a 3-month study of a solid dose formulation of calcium acetate; all cases resolved upon lowering the dose or discontinuing treatment. Maintain the serum calcium-phosphorus product (Ca X P) below 55 mg^2/dL^2.

Concomitant Use with Medications. Hypercalcemia may aggravate digitalis toxicity. Phoslyra contains maltitol (1 g per 5 mL) and may induce a laxative effect, especially if taken with other products containing maltitol.

ADVERSE REACTIONS: No clinical trials have been performed with Phoslyra in the intended population. Because the dose and active ingredients of Phoslyra are equivalent to that of the calcium acetate gelcaps or tablets, the scope of the adverse reactions is anticipated to be similar.

Hypercalcemia is discussed elsewhere *[see Warnings and Precautions]*.

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

In clinical studies, calcium acetate has been generally well tolerated.

The solid dose formulation of calcium acetate was studied in a 3-month, open-label, non-randomized study of 98 enrolled ESRD hemodialysis patients and in a two week double-blind, placebo-controlled, cross-over study with 69 enrolled ESRD hemodialysis patients. Adverse reactions (>2% on treatment) from these trials are presented in Table 1.

Table 1: Adverse Reactions in Patients with End-Stage Renal Disease Undergoing Hemodialysis

	Total adverse reactions reported for calcium acetate n=167	3-mo, open-label study of calcium acetate n=98	Double-blind, placebo-controlled, cross-over study of calcium acetate n=69	
			Calcium acetate	Placebo
Preferred Term	n (%)	n (%)	n (%)	n (%)
Nausea	6 (3.6)	6 (6.1)	0 (0.0)	0 (0.0)
Vomiting	4 (2.4)	4 (4.1)	0 (0.0)	0 (0.0)
Hypercalcemia	21 (12.6)	16 (16.3)	5 (7.2)	0 (0.0)

Calcium acetate oral solution was studied in a randomized, controlled, 3-arm, open label, cross-over, single-dose study comparing calcium acetate oral solution to a solid formulation in healthy volunteers on a controlled diet. Of the observed drug-related adverse reactions, diarrhea (5/38, 13.2%) was more common with the oral solution.

Postmarketing Experience. The following additional adverse reactions have been identified during post-approval of calcium acetate: dizziness, edema, and weakness.

DRUG INTERACTIONS: The drug interaction profile of Phoslyra is characterized by the potential of calcium to bind to drugs with anionic functions (e.g., carboxyl, carbonyl, and hydroxyl groups). Phoslyra may decrease the bioavailability of tetracyclines or fluoroquinolones via this mechanism.

There are no empirical data on avoiding drug interactions between calcium acetate or Phoslyra and most concomitant drugs. When administering an oral medication with Phoslyra where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, administer the drug one hour before or three hours after Phoslyra or calcium acetate. Monitor blood levels of the concomitant drugs that have a narrow therapeutic range. Patients taking anti-arrhythmic medications for the control of arrhythmias and anti-seizure medications for the control of seizure disorders were excluded from the clinical trials with all forms of calcium acetate.

Ciprofloxacin. In a study of 15 healthy subjects, a co-administered single dose of 4 calcium acetate tablets (approximately 2.7 g) decreased the bioavailability of ciprofloxacin by approximately 50%.

USE IN SPECIFIC POPULATIONS

Pregnancy: Category C. Phoslyra contains calcium acetate. Animal reproduction studies have not been conducted with Phoslyra, and there are no adequate and well controlled studies of Phoslyra use in pregnant women. Patients with end stage renal disease may develop hypercalcemia with calcium acetate treatment *[see Warnings and Precautions]*. Maintenance of normal serum calcium levels is important for maternal and fetal well being. Hypercalcemia during pregnancy may increase the risk for maternal and neonatal complications such as stillbirth, preterm delivery, and neonatal hypocalcemia and hypoparathyroidism. Phoslyra treatment, as recommended, is not expected to harm a fetus if maternal calcium levels are properly monitored during and following treatment.

Labor and Delivery. The effects of Phoslyra on labor and delivery are unknown.

Nursing Mothers. Phoslyra contains calcium acetate and is excreted in human milk. Human milk feeding by a mother receiving Phoslyra is not expected to harm an infant, provided maternal serum calcium levels are appropriately monitored.

Pediatric Use. Safety and effectiveness of Phoslyra in pediatric patients have not been established.

Geriatric Use. Clinical studies of calcium acetate 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, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

OVERDOSAGE: Administration of Phoslyra in excess of the appropriate daily dosage may result in hypercalcemia *[see Warnings and Precautions]*.

HOW SUPPLIED/STORAGE AND HANDLING: Phoslyra for oral administration is a clear solution containing 667 mg calcium acetate per 5 mL. Phoslyra is supplied in a 473 mL (16 oz) amber-colored, multiple-dose bottle, packaged with a marked dosing cup. Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature]. The shelf life is 24 months.

PATIENT COUNSELING INFORMATION: Inform patients to take Phoslyra with meals, adhere to their prescribed diets, and avoid the use of calcium supplements including nonprescription antacids. Inform patients about the symptoms of hypercalcemia *[see Warnings and Precautions and Adverse Reactions]*.

Advise patients who are taking an oral medication where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy to take the drug one hour before or three hours after Phoslyra.

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101493-01 Rev. B 08/2012

ASN Crafts Roadmap for Diversity and Inclusion

In 2013, ASN organized a summit in Washington, DC, to help leaders develop a proposal for increasing diversity at all levels of the society, particularly in terms of those underrepresented in medicine. At ASN's Diversity Summit, led by Dr. Donald Wesson and Dr. Jonathan Himmelfarb, participants reviewed results of a survey of senior leaders in nephrology and diversity and developed recommendations that were presented to, and unanimously approved by, ASN Council in August 2013. These recommendations are being enacted with the oversight of ASN's Diversity and Inclusion Work Group (Table 1), a new working group developed to directly address diversity issues at ASN, and by ASN's Diversity Champion, Dr. Eddie Greene.

Diversity (a range of difference and variety) and inclusion (bringing all parts into the whole) advance an organization's success, reach, and competitiveness. Organizations that embrace diversity and inclusion are more effective at strategic development and execution, and at applying a variety of skills and experiences to achieve optimum results. In addition, the patient population in nephrology is disproportionately minority, and will be better served by a more diverse nephrology workforce.

ASN's focus on diversity: beyond the moral imperative

ASN is well positioned and committed to playing a critical role in the multiple events impacting the fight against kidney disease. These include health care reform, evolving national demographics, economic challenges, advances in translational science, and potential changes in the nephrology workforce. Incorporating a framework of diversity and inclusiveness optimizes ASN's capacity to achieve excellence in the entire scope of its mission—supporting education, advocating for high quality care, communication, and research. The engagement of multiple perspectives, skill sets, and experiences will strengthen ASN's national and global leadership (Nivet, Diversity 3.0 Commentary Academic Med, 86, 2011, Diversity 5.0, CT Laurencin, IOM).

Diversity Roadmap: a marathon, not a sprint

To begin to build a more diverse and inclusive organization, minority ASN nephrologists met in June 2013 at the society's office to draft foundational initiatives and recommendations that were then approved for implementation by ASN Council (Table 2). ASN then convened the Diversity and Inclusion Work Group in late 2013 to help ASN develop a roadmap for improving diversity and inclusion. In addition, ASN Council appointed Dr. Eddie Greene as Diversity Champion. Dr. Greene reviews all ASN activities (not just those of the Work Group) and reports to ASN Council regarding the society's progress in improving diversity and inclusion across all aspects of the society. Incoming ASN President Dr. Jonathan Himmelfarb and Dr. Donald Wesson co-chair the Diversity and Inclusion Work Group.

Diversity and Inclusion Work Group recommendations

In developing the diversity roadmap for ASN, the work group crafted a mission statement that was reviewed and approved by the Council. The resulting diversity and inclusion mission statement is the first for ASN and sets the stage for ongoing activities and recommendations. The work group also actively supported a Kidney Week lectureship that honors the late Michelle P. Winn, MD, who contributed substantially to genetics research in nephrology, additional collection of demographic data from ASN members, development of web resources for increasing diversity, and promotion of diversity among ASN leadership.

Metrics, accountability, and you

With key input from the work group, in January 2014 ASN expanded its options for collecting demographic information from members, including information about types of practice, professional appointments, as well as race and ethnicity. The Diversity and Inclusion Work Group will evaluate demographic shifts over time to assess the performance of the growing array of initiatives aimed at broadening diversity in ASN and within nephrology. **If you have not already filled out this information, we urge you to do so when you renew your membership at http://www.asn-online.org/membership/.**

The road forward

Diversity and inclusion are key components of an organization striving for excellence. ASN's commitment to embedding diversity in the fabric of the organization reflects this, as well as the moral imperative of addressing health care disparities, unequal access, and discrimination that have existed in the health care system.

Led by the guiding principles of its statement on diversity and inclusion, ASN will effect change by promoting inclusiveness, mentorship, patient advocacy, engagement, and health equity. ASN President Sharon Moe, MD, FASN, notes "ASN is grateful to the members of the Diversity and Inclusion Work Group, and to Dr. Greene in his role as Diversity Champion, for their energy, creativity, and thoughtfulness; their work has already enhanced the activities of ASN and will, ultimately, help improve care for kidney patients."

Recommendations approved by ASN Council

1. Increase representation of underrepresented minorities as leaders across all ASN committees, advisory groups, and panels, as well as ASN Council (and consider mentored ad-hoc positions to provide exposure to ASN leadership activities at earlier stages in career development).
2. Develop partnerships with other highly effective organizations that have successful diversity and inclusion and minority outreach programs.
3. Establish a sustainable and highly effective mentoring program.
4. Create strong career development and training resources.
5. Reconfigure ASN's website to include a focus on diversity and inclusion and related mentoring opportunities.
6. Develop baseline data on ASN member demographics and structured mechanisms for tracking diversity and inclusion across all ASN activities.

Table 1

ASN Diversity and Inclusion Work Group

Co-Chairs
Jonathan Himmelfarb, MD, FASN
Donald E. Wesson, MD, FASN

ASN Diversity Champion
Eddie L. Greene, MD

Members
Deidra C. Crews, MD, FASN
Crystal A. Gadegbeku, MD
Keisha L. Gibson, MD
Kevin O. Griffiths, MD, FASN
German T. Hernandez, MD, FASN
Robert S. Hoover, Jr., MD, FASN
Kalani L. Raphael, MD
Bessie A. Young, MD, FASN

Table 2

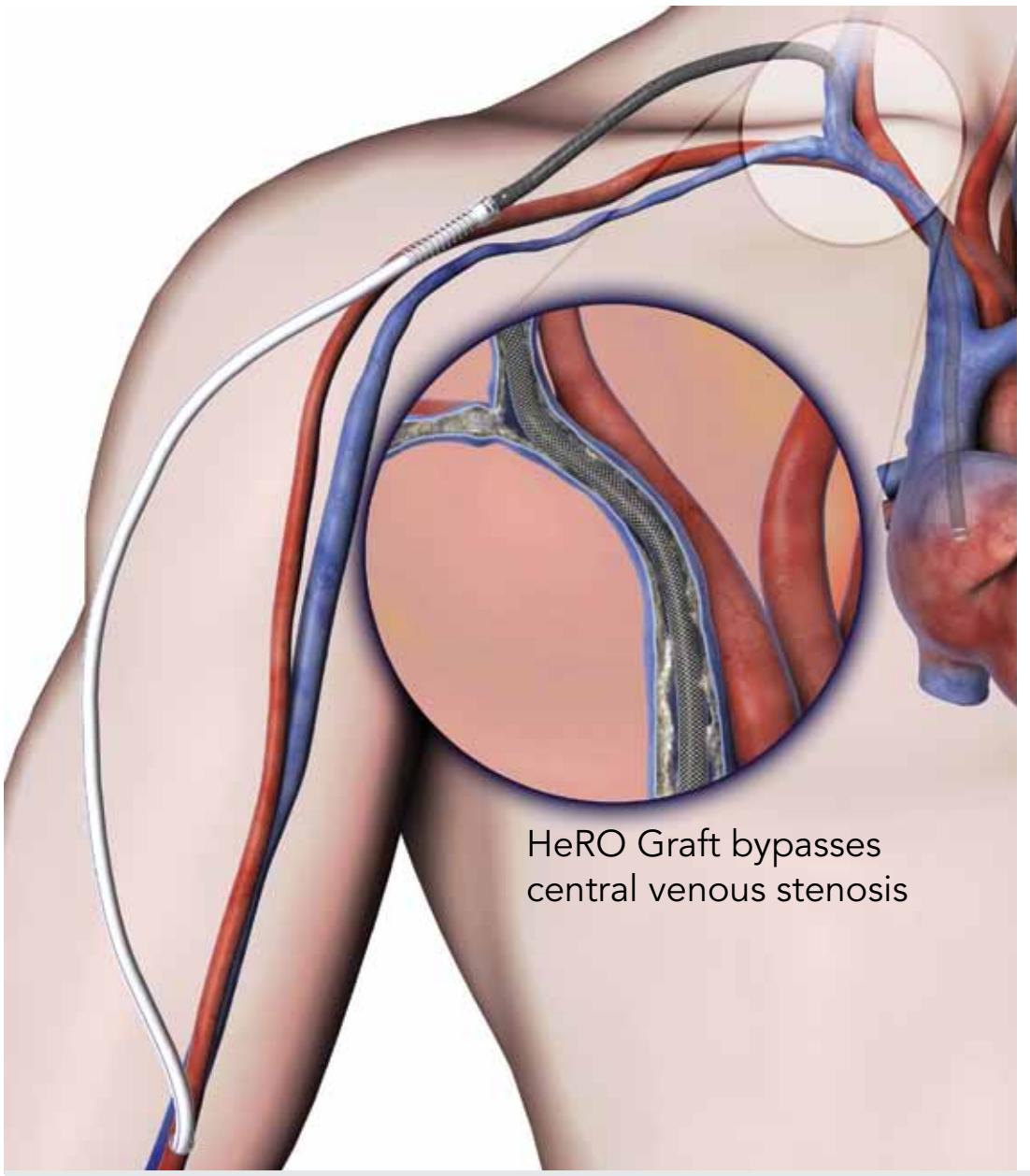
Mission, vision, and values

Mission
The American Society of Nephrology will promote diversity and inclusiveness to enhance the nephrology profession and the lives of people with kidney disease through improved health care, research, and education.

Vision
A diverse and inclusive ASN will foster innovation, creativity, and sensitivity to advance health for all people living with kidney disease and serve as a model for organizations dedicated to health equity.

Values
The values here serve as guiding principles to effect positive change in ASN, the profession of nephrology, and the lives of people with kidney disease.

- Inclusiveness: Promote and encourage contributions and collaboration among colleagues.
- Mentorship: Improve career opportunities for professionals dedicated to curing kidney disease.
- Health Equity: Work strategically to eliminate disparities in the diagnosis and treatment of kidney disease.
- Patient Advocacy: Advocate for universal access to quality care for all people living with kidney disease.
- Engagement: Support civic engagement and community service as part of the professional experience.



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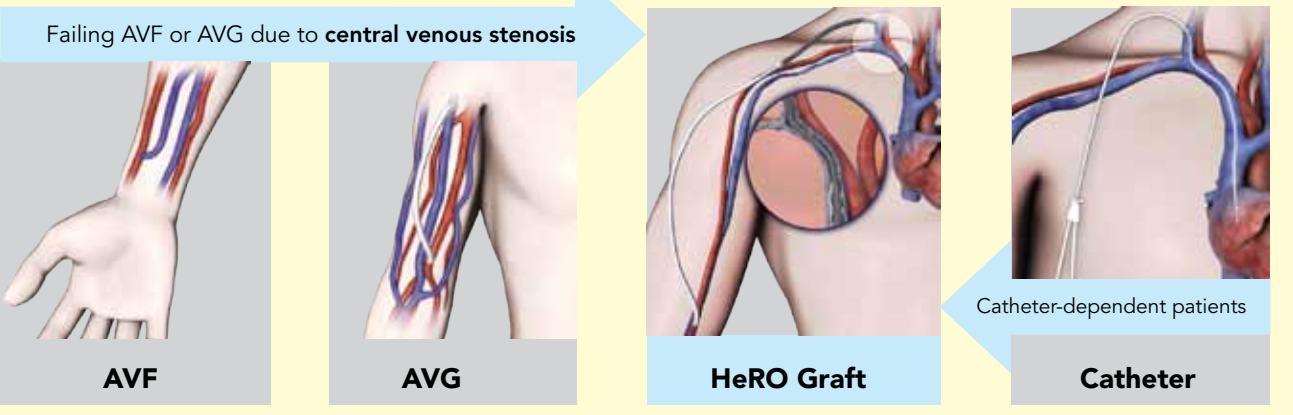

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References:
1) Katzman et al., J Vasc Surg 2009. 2) Gage et al., EJVES 2012. 3) Dageforde et al., JSR 2012.

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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20 Things to Know about Your ASN

A Look at ASN's Activities Since Kidney Week 2013

1. ASN is overseeing a detailed analysis of the **Nephrology Workforce**. The society contracted with a team from George Washington University in Washington, DC, to evaluate data from multiple sources to determine the composition and practice patterns of the current workforce, the subspecialty's evolving clinical role in health care, potential effects of recent policy changes on nephrology practice, and potential market trends in the future.

2. ASN invited 219 medical students, graduate students, and residents to participate in the 2014 **Kidney STARS** program (formerly known as the ASN Program for Students and Residents). The society received 998 applications for travel support from students, residents, fellows, and other trainees and funded 366 trainees (including the 219 Kidney STARS) to attend Kidney Week 2014.

3. ASN partnered with Mount Desert Island Biological Laboratory to provide 30 medical and graduate students a weeklong experience in the "Origins of Renal Physiology." **Kidney TREKS** (Tutored Research and Education for Kidney Scholars) also promotes ongoing mentorship at the students' medical or graduate schools as well as travel support to Kidney Week.

4. The ASN **Diversity and Inclusion** Work Group is gathering more demographic information from ASN members, including data on race and ethnicity. The society encourages members to provide this information when they renew their membership. The work group is developing strong baseline data to evaluate the success of ASN's commitment to diversity and inclusion.

5. Assessing the impact of the ASN Career Development Grants Program, "The Kidney Research Predicament" concluded that ASN-funded grant recipients "are making significant contributions to disseminating nephrology research." Since 1996, ASN has invested more than $19 million in career development grants, enabling nearly 120 investigators to conduct original, meritorious research. Besides funding up to 20 career development grants annually, the **ASN Foundation for Kidney Research** also funds 20 nephrology fellows and 10 medical students each year.

6. The ASN Foundation for Kidney Research also launched the **William and Sandra Bennett Clinical Scholars Program**. Established by former ASN President and founding Editor-in-Chief of the *Clinical Journal of the American Society of Nephrology (CJASN)* William M. Bennett, MD, FASN, and wife Sandra, the program will support two aspiring kidney educators annually to conduct projects to advance all facets of nephrology teaching.

7. ASN helped spearhead successful efforts to pass the HOPE (HIV Organ Policy Equity) Act of 2013. ASN also organized the 2014 Kidney Community Advocacy Day, uniting more than 100 representatives from 14 patient and professional organizations to conduct 133 meetings with members of the **U.S. Congress** and their staffs in support of research funding and immunosuppressive drug access. Efforts to ensure the highest quality care for kidney patients also paid dividends: Several **Medicare** programs implemented ASN recommendations, including making home dialysis more accessible, eliminating unnecessary quality measures, and protecting access to Part D drugs and dialysis care for hospice patients.

8. ASN launched a **Research Advocacy Strategy** that seeks an additional $150 million per year over 10 years for kidney research above current U.S. federal government funding—a request supported by nearly 35 other organizations. Congressional Kidney Caucus Co-Chair Rep. Tom Marino (R-PA) called for a report to Congress on the adequacy of federal investment in kidney research. ASN President Sharon M. Moe, MD, FASN, testified before the U.S. House of Representatives Committee on Science, highlighting the lack of innovation and need for better therapies. Dr. Moe testified that a prize competition could harness the power of the private and academic sectors to spur breakthroughs in care.

9. ASN convened a **Summit for Community Nephrologists**. Participants provided key information that will help inform ASN policy initiatives and improve the annual meeting experience for all health professionals. The summit also provided valuable insights into current and future workforce initiatives. For example, ASN will explore opportunities to help nephrologists incorporate new technologies, maximize application of electronic health records, and incorporate telehealth into practice.

10. The Summit for Community Nephrologists is part of a three-year effort to strengthen ASN's relationships with its many **Internal and External Constituencies**. In 2013, the society held summits for underrepresented minorities, for PhDs, and organized the first Summit of U.S. Kidney Organizations. This year, ASN has organized a second Summit of U.S. Kidney Organizations and a Forum of International Kidney Organizations, which will both take place during Kidney Week. ASN, the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA), and the International Society of Nephrology (ISN) held a leadership retreat in June and are planning a follow-up meeting in January 2015.

11. ASN joined other specialty societies and the American College of Physicians to raise concerns about **Maintenance of Certification (MOC) 2014**, which the American Board of Internal Medicine (ABIM) introduced in January. Changes to the program are intended to make MOC a more continuous process throughout the 10-year certification cycle, spreading recertification requirements more evenly. The entire internal medicine community was confused about these changes and an overhaul of ABIM's governance structure.

12. ASN implemented the Accreditation Council for Graduate Medical Education (ACGME) Next Accreditation System (NAS) Internal Medicine Subspecialty Reporting Milestones for fellowship training and implemented **Nephrology Curricular Milestones** and entrustable professional activities (EPAs) on July 1. NAS moves each specialty toward continuous accreditation through developing outcomes-based milestones as a framework for determining resident and fellow performance within the six ACGME Core Competencies.

13. ASN will present the **Inaugural Michelle P. Winn Endowed Lectureship** during Kidney Week 2014. Focused on glomerular diseases and genetics, the endowed lecture honors Dr. Winn, a generous mentor, respected clinician, and admired physician-scientist. In 2007, Dr. Winn received the Young Investigator Award from ASN and the American Heart Association.

14 In 2014, ASN focused its regional version of Kidney Week—called **ASN Highlights**—outside the United States. ASN Highlights were held in Amsterdam as part of the ERA–EDTA Congress; Santiago, Chile, in cooperation with the Sociedad Latinoamericana de Nefrología e Hipertensión; and Berlin, with the German Society of Nephrology. ASN Highlights will take place in at least six countries in 2015, including Brazil, Germany, Mexico, South Africa (as part of ISN's World Congress of Nephrology), United Kingdom (as part of the ERA–EDTA Congress), and the United States (in Chicago, Houston, and Orlando).

15 The Nephrology Self-Assessment Program **(NephSAP)** moved from print to online. This move allowed NephSAP to expand its unparalleled educational content for kidney professionals as well as offer an array of new features to enhance learning. The new version offers easier access, personalized options, and integration features.

16 ASN recently completed a search process for the next Editor-in-Chief of ASN ***Kidney News.*** Pascale H. Lane, MD, FASN, has built *Kidney News* into ASN's largest-circulation publication, and ASN is very grateful for her incredible achievements. Richard A. Lafayette, MD, has been appointed Editor-in-Chief and will begin his term January 1, 2015.

17 The **Impact Factors** for the *Journal of the American Society of Nephrology (JASN)* and *CJASN* continue to increase. *JASN* rose from 8.98 to 9.46, and *CJASN* grew from 5.068 to 5.25. *JASN* remains the number one cited journal in nephrology. The 2013 impact factor (released in July 2014) is based on the number of citations made in 2013 to articles published in 2011 and 2012.

18 A partnership between ASN and the Food and Drug Administration (FDA)—that includes 68 member organizations from around the world—the **Kidney Health Initiative (KHI)** continues to achieve its mission of enhancing patient safety and fostering innovation in kidney disease. Representatives from ASN, FDA, and other KHI members met in June for the second annual stakeholders' meeting, and KHI has initiated eight projects since its creation in September 2012.

19 Of ASN's 14,928 members, 6184 (41 percent) are from outside the United States, representing 115 countries. On average, 45 percent of the participants at Kidney Week are from outside the United States, and 2715 (56 percent) of the 4864 abstracts submitted for Kidney Week 2014 were submitted from outside the United States. During the past 12 months, *JASN* and *CJASN* received 58 percent and 68 percent, respectively, of submissions from outside the United States; 66 percent of journal subscriptions, 75 percent of Facebook followers, and 45 percent of Twitter followers are from **Around the Globe**.

20 **Coming Soon**, ASN will convene a "blue ribbon panel" to focus on career development, mentoring, and sponsorship to expand support for future generations of kidney professionals; add the Kidney Transplantation Practice Improvement Module (in partnership with the American Society of Transplantation), launch the Kidney Self-Assessment Program, which have already been approved by ABIM; and finalize a new strategic plan.

ASN President Sharon M. Moe, MD, FASN, Reflects on Year's Accomplishments

Sharon M. Moe

What has ASN accomplished this year?

It has been a busy year, and I have been honored to work with ASN's councilors, committees, and advisory groups on many important projects.

The ASN has aggressively worked to identify barriers to interest in nephrology and to overcome those barriers through multiple initiatives targeting medical students and residents. The Workforce Committee, led by Mark Parker, MD, has implemented new programs to combat misconceptions about, and promote the many rewards of, nephrology careers. These programs will be visible at ASN Kidney Week 2014, and I encourage every ASN member to spend time with students, residents, and fellows discussing their research, their careers, and why they became passionate about kidney health. We are our own best advocates for nephrology!

The Training Program Directors Executive Committee, chaired by Nancy Adams, MD, has developed nephrology fellowship milestones for the new United States trainee evaluation criteria. This amazing feat was accomplished in a very short time, and I am grateful for their contributions. These milestones align evaluations across the country and will allow better characterization of training programs and ensure that the fellows master critical skills.

Research advocacy remains an important mission for ASN, especially in the current scientific funding environment. In the United States, kidney disease is disproportionately underfunded, given the high prevalence of, and high cost of care for, kidney disease. ASN's aggressive research strategic plan emphasizes these two important points to congressional leaders.

The ASN worked with the congressional kidney caucus to request a formal Government Accountability Office report to substantiate the imbalance between prevalence and cost of kidney disease versus research funding to find a cure for kidney disease. Caring for patients with ESRD is a major cost for health care systems everywhere. Research is needed to identify the causes of kidney diseases, to characterize why some patients progress and others do not, and to determine how some of the identified genes in minority populations increase progression. Clearly, we have a lot to learn, and research is necessary if we hope to improve lives and contain the costs of caring for this population in the future.

The ASN is also advocating for innovation in dialysis delivery because current modalities have not significantly changed in the past 30 years. I was honored to testify before the House Science Subcommittee on Research and Technology about this lack of innovation and the need for better therapies. This testimony, and subsequent meetings with Congress and regulatory agencies, raised awareness about the importance of fostering new therapies to give patients receiving dialysis a better quality of life at a lower cost.

Other fields have made such advances, and I know that nephrology investigators are equally talented. Real innovation is in the foreseeable future, but it requires harnessing the immense talent within the nephrology community and collaborating with investigators and bioengineers beyond the traditional kidney research sphere. The increased impact factor of our journals and the high quality of published research are just one indication that scientists are paying attention to our specialty.

The ASN continues to advocate within the Centers for Medicare & Medicaid Services to ensure that health care delivery to our patients is optimized and reimbursed appropriately. We support high-quality care, but we also want to ensure that the metrics that measure quality reflect improved outcomes. Health care delivery models are changing rapidly, and, as usual, nephrology has been ahead of other medical specialties in the United States, implementing the first-ever disease-specific Accountable Care Organization program in Medicare. ASN worked closely with Medicare and others in the kidney community to ensure the success of this novel care delivery model. As we move forward we need to protect our profession and continue to provide high-quality continuity of care across the spectrum of kidney diseases and the many health care delivery settings.

Such dynamic changes require building new paths to improve patient care and working with teams of caregivers in multiple settings. These teams must be diverse and well trained, and ASN is dedicated to ensuring that both of these goals are met. ASN Diversity Champion Eddie Greene, MD, will provide an external review of ongoing ASN efforts to diversify our membership and leadership. A series of summits has helped identify barriers to engagement, areas for improvement, and future opportunities.

What did you like best about being ASN president?

It has been a pleasure to work with the outstanding ASN staff and to help set the society's priorities for this and coming years as we initiated ASN's new five-year strategic planning efforts. These are challenging times, with shifts in health care delivery, reduced research funding, and changing educational requirements. Each poses a threat to nephrology, and we must continue to be proactive in turning these challenges into opportunities. I have been honored to lead these efforts.

What surprised you about being ASN president?

What surprised me most is the importance of short conversations with members of Congress, their staffs, and other government officials. I wasn't expecting to meet so many stakeholders, but it has been exciting to do so. These interactions raise awareness about kidney disease, the importance of research, and the need for innovations in all aspects of kidney care.

What advice do you have for others in the nephrology community?

We need to be proactive and positive in promoting nephrology to the public, students, politicians, and government. Nephrology offers physicians a rewarding career that combines the excitement of science and physiology, continuity of care and lasting relationships, and the opportunity to improve our patients' lives. We are detail-oriented by necessity, but sometimes this attention to detail can become unnecessarily negative. I encourage everyone to think positively and embrace collaboration in research, innovation, education, and health care delivery across the kidney health spectrum. The ultimate goal is to improve the care of those with kidney disease. ASN Kidney Week is a great forum for expanding and initiating collaborations with colleagues from around the world. Together we can make a difference, but we need to embrace change, rise to the challenges before us, and encourage one another.

What will you not miss once you are past president?

I won't miss the frequent trips to Washington, DC. I have the times for all the direct flights memorized!

What other question should we have asked you?

I would like to thank ASN's staff, especially executive director Tod Ibrahim. These amazing groups of talented and hard-working individuals believe that kidney disease can be cured, and their enthusiasm is infectious. I also thank my husband, John, and daughter, Michelle, for their patience and support this year. Finally, I thank ASN's members for the honor of serving as your president.

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ASN President-Elect Jonathan Himmelfarb, MD, FASN, Looks to the Year Ahead

Jonathan Himmelfarb

What issues do you anticipate being big in the coming year as ASN President?

Without a doubt the coming year will present many exciting opportunities and challenges for nephrology, and I anticipate that ASN will be right in the middle of the action. There will continue to be volatility with respect to the reorganization of health care delivery, and nephrology always seems to be front and center in the assessment of quality metrics, in the bundling of payments for cost control, and in demonstrating value in comprehensive, team-based specialty care.

The strong trend in health care is toward integrated care models, which will likely result in more and more consolidation among hospital networks, and perhaps dialysis providers. In this rapidly changing environment, ASN will be working hard to emphasize the value of nephrology care to patients and to health care systems. Over time nephrology may shift from the traditional hospital- and clinic-centric approach, which is essentially passive, episodic, and disease oriented (waiting for the patient), toward more technology-enabled, population management strategies. Our goal is for ASN to help make the case that kidney care provides essential value within these increasingly integrated care models.

On the education and communications fronts, ASN will continue to develop innovative products that meet members' needs, including new self-assessment tools that make it easier to maintain certification. As an example, ASN plans to roll out KSAP (Kidney Self-Assessment Program), an exciting addition to materials that help nephrologists prepare for board exams.

The kidney community is also observing seismic shifts in the research landscape. Having been active in a wide variety of clinical and translational research efforts over the past 25 years, I see the coming era as providing the opportunity for true breakthroughs that can substantively change outcomes for people living with kidney disease. Yet at the same time, we are experiencing funding challenges that threaten to stall or even prevent progress. Despite many serious funding problems, especially for young investigators, the research tools available are unprecedented, and as a research community we are learning how best to use them, especially through collaborative, multidisciplinary, and often multi-institutional approaches. The scientific enterprise is now truly global, a trend that will likely accelerate in the coming year.

What do you particularly look forward to doing?

I am very excited about what ASN can do to develop tools and resources to support nephrologists and kidney scientists in every stage of their careers. I particularly want to find ways to help younger nephrologists navigate the landscape of clinical practice, learn to become great educators, and become successful researchers who will change the future practice of nephrology. We need to implement strategies to strengthen the pipeline of future leaders in our field.

Most of all, I am excited that ASN has begun a journey to become a more diverse, open, and inclusive organization. ASN has embarked on an initiative to increase diversity and inclusion at all levels of the organization, including (but certainly not limited to) gender, racial, and ethnic diversity. We need to take advantage of all the talent in our field to maintain our successes. This is especially critical given the patient population we serve. We need for our entire community to feel valued and capable of participating in the work of ASN. This can only make ASN a stronger and better organization. Membership also must be inclusive, and as part of this effort we need to reach out to each member of the care delivery team who contributes to kidney disease care.

Are there any parts of the job you are dreading?

To be honest, because I really care deeply about ASN, I look forward to taking on this leadership role with almost no reservations. Over the past three decades I have been involved in almost all aspects of the ASN core missions, including education, communications, public policy, and research activities. So I feel as though I understand the organization well and am well aware of the change dynamic within the society and the broader kidney community. Yet at the same time I do realize the level of required time commitment for this role. If there is anything I dread it is the required travel, especially the frequent trips from Seattle to the East Coast and beyond. This year I achieved diamond status for frequent flier miles (not something to be proud of), and I suspect next year will be worse.

You have significant policy experience. How will that experience influence your year as ASN president?

As the inaugural Chair of ASN's Public Policy Board before becoming a Councilor, I learned a lot about how best to collaborate with organizations external to ASN, to help further ASN's mission and goals. This collaboration is essential, given the high prevalence and complexity of kidney disease, which touches so many individuals and organizations.

Policy informs many of the daily activities within ASN. As an example, ASN will continue to dialogue with and reach out to the many patient advocacy organizations that care about kidney disease in order to increase our community's effectiveness in getting the word out about the importance of kidney disease to public health in North America and worldwide.

Patients are our partners in spreading the word about the need for optimal clinical care and for innovation through research that can change clinical care for the better. An outstanding recent example is the Kidney Health Initiative (KHI), an effort led by ASN in partnership with the FDA. Now comprised of 68 member organizations, KHI works to remove barriers to innovation in developing new safe, effective medical products for treatment of kidney disease.

Being involved in policy has taught me that ASN must be proactive in trying to solve problems, and ASN must understand the political, legislative, and regulatory environment to be an effective organization.

Time out.

Let’s take a moment to look at the current state of the lab industry.

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KIDNEY HEALTH INITIATIVE

KHI's Collaborative Approach Identifies Priorities and Opportunities That Will Have an Impact on Kidney Disease

Despite the large number of Americans affected by kidney disease, few new drugs have been approved to treat it in the past decade. To address this issue and to ensure high-quality care for every patient with kidney disease, the American Society of Nephrology (ASN) and the U.S. Food and Drug Administration (FDA) formed a public–private partnership called the Kidney Health Initiative (KHI) in September 2012 to enhance patient safety and foster innovation.

Over the past 2 years, KHI has made advances toward fulfilling its mission through a collaborative partnership with the kidney community. In particular, the KHI board of directors would like to thank its 68 members for their commitment, ideas, and participation in the annual stakeholders' meetings and in project workgroups.

As a member-driven initiative, KHI meets its mission and objectives through the completion of projects proposed by members across the kidney community, including the FDA, organizations of patients, organizations of health professionals, research institutions, and members of industry, including small and large pharmaceutical, biotechnology, and device companies along with dialysis organizations. The focus of KHI is to promote innovation within the kidney space, but also core to its mission is innovation within the process of project selection, work group constitution, and deliverables.

These innovations include (a) creation of a precompetitive, multidisciplinary platform where all the stakeholders can come together and interact, (b) special emphasis on patients and their views on how to improve kidney care, (c) an opportunity for all interested members to participate in the project work groups, (d) collaborative relationships with federal agencies such as the FDA, the Centers for Medicare and Medicaid Services, the National Institutes of Health, and the Centers for Disease Control, and (e) emphasis on the project *deliverables* being *enablers* such as white papers, workshops, and data standards that would likely allow for a long-term impact on innovation by creating a durable and well-accepted "pathway for innovation."

KHI's early progress gives kidney patients hope for a better tomorrow and emphasizes that real advances can be made through a collaborative approach that brings together all the stakeholders in the kidney space.

Currently, five active ongoing projects within KHI are focusing on a wide range of kidney-relevant topics, ranging from continuous renal replacement therapy pharmacokinetics to vascular access to lupus nephritis (Table 1). In addition, the KHI board recently endorsed an additional four projects on data standards for diabetic nephropathy, pragmatic trials in nephrology, regulatory policies and positions for device approval, and advancing technologies for patient self-care in the setting of renal replacement therapy. The deliverables from these nine projects will include workshops, white papers, and data standards. We believe that these outputs will then serve as a platform (as an enabler) for further much-needed progress in these areas.

The identification of a set of well-defined, scientifically validated clinical trial endpoints for lupus nephritis and dialysis vascular access, for example, could greatly facilitate clinical trials of innovative therapies for both these conditions, which would likely translate into improved care for patients with chronic kidney disease and ESRD.

KHI's early progress gives kidney patients hope for a better tomorrow and emphasizes that real advances can be made through a collaborative approach that brings together all the stakeholders in the kidney space.

KHI looks forward to continued growth and interaction among its diverse members. To obtain additional information or discuss KHI and its projects, please contact the KHI staff at KHI@asn-online.org.

Table 1. Kidney Health Initiative Ongoing Projects

KHI Project	Representatives	Problem	Objective	Deliverable
Pharmacokinetics in Patients Receiving Continuous Renal Replacement Therapy (CRRT)	• Nephrologists • Clinical pharmacologists • FDA Office of Clinical Pharmacology • NIDDK • Industry Led by: T. Nolin, G. Aronoff, S. Goldstein	There is a paucity of clinical data regarding the effect of acute kidney injury (AKI) and modern CRRT methods on drug exposure and response.	1. Prioritize drugs/drug classes with regard to importance of generating clinical data. 2. Propose pertinent study design issues, with emphasis on those that distinguish CRRT from intermittent hemodialysis. 3. Recommend practical considerations in the conduct, analysis, and reporting of results.	Publication in *CJASN* Workshop on Tuesday, November 11
Innovative Treatments for Kidney Disease: Barriers and Solutions	• Patient • Industry • Nephrologists • FDA • CMS Led by: P. Linde	Lack of innovation and incentive for discovery results in a deficiency in the development of new therapies. There is also a lag in establishing an evidence base to promote scientific advancement for patients with CKD.	1. Define major barriers to innovation in kidney health. 2. Propose solutions that emphasize collaborative approaches among stakeholders.	Publication
Endpoints: Lupus Nephritis	• Nephrologists • Rheumatologists • Statisticians • FDA Led by: B. Rovin	Despite successful completion of several large-scale, controlled clinical trials in lupus nephritis, there has yet to be an FDA-approved drug for the treatment of lupus nephritis. Lack of clarity about choice of outcome measures and definitions of response criteria have likely contributed to this situation.	1. Recommend a core set of outcome measures, biomarkers, and surrogate markers. 2. Define clear terms that should be incorporated into all lupus nephritis trials.	Publication
Identify Patient Preferences to Support Device Regulatory Actions	• Patients • Patient advocates • FDA Center for Devices and Radiological Health • Industry Co-chairs: D. Chianchiano, F. Hurst	CDRH emphasized the importance of incorporating patient preferences into product development programs and into regulatory decision-making, but the relevant stakeholders (industry, patients, and regulators) have an imperfect understanding of best practices for creating the tools to capture and analyze data related to patient preferences.	1. Convene a workshop where regulators, the device industry, and patient advocacy groups can discuss barriers and solutions to developing tools to facilitate the incorporation of patient preferences into product development and regulatory decision-making	Workshop
Endpoints: Dialysis Vascular Access	• FDA • Industry • Nephrologists • Surgeons Co-chairs: M. Wasse, S. Shenoy	There are currently no truly effective therapies for dialysis vascular access dysfunction. One possible reason is the lack of well described clinical trial endpoints for novel therapies in the vascular access field.	1. Clarify appropriate endpoints for vascular access trials best suited to inform clinical, regulatory, and coverage decisions, where clinical data are required to support the decisions	Workshop Publication

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ADVERSE REACTIONS: Most commonly reported adverse reactions (≥5%) are vomiting, abdominal pain/discomfort, headaches, nausea, diarrhea, anorexia/decreased appetite, breath odor, fatigue, dizziness, skin odor, and rash.

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The following is a brief summary of the full prescribing information and does not include all of the information needed to use PROCYSBI safely and effectively. See full prescribing information for PROCYSBI.

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Initial U.S. Approval: 1994

INDICATIONS AND USAGE

PROCYSBI is a cystine-depleting agent indicated for the management of nephropathic cystinosis in adults and children ages 6 years and older (see Section 1 of the full prescribing information).

CONTRAINDICATIONS

- **Hypersensitivity to penicillamine (see Section 4 of the full prescribing information).**

WARNINGS AND PRECAUTIONS

- **Monitor for development of skin or bone lesions and reduce dosage of PROCYSBI if necessary (see Section 5.1 of the full prescribing information).**
- **If a severe skin rash develops such as erythema multiforme bullosa or toxic epidermal necrolysis, PROCYSBI should be discontinued (see Section 5.2 of the full prescribing information).**
- **Monitor for symptoms of gastrointestinal ulceration and bleeding (see Section 5.3 of the full prescribing information).**
- **Monitor for central nervous system (CNS) symptoms such as seizures, lethargy, somnolence, depression, and encephalopathy (see Section 5.4 of the full prescribing information).**
- **Cysteamine has been associated with reversible leukopenia and abnormal liver function levels. Therefore, white blood count and elevated alkaline phosphatase levels should be monitored (see Section 5.5 of the full prescribing information).**
- **Monitor for signs and symptoms of benign intracranial hypertension (see Section 5.6 of the full prescribing information).**

ADVERSE REACTIONS

Most commonly reported adverse reactions (≥5%) are vomiting, abdominal pain/discomfort, headaches, nausea, diarrhea, anorexia/decreased appetite, breath odor, fatigue, dizziness, skin odor, and rash (see Section 6.1 of the full prescribing information).

Please visit PROCYSBI.com for the Full Prescribing Information.

Reference: 1. PROCYSBI [package insert]. Novato, CA: Raptor Pharmaceuticals Inc; 2014.

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- **Pregnancy: Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. PROCYSBI should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (see Section 8.1 of the full prescribing information).**
- **Nursing Mothers: Breastfeeding is not recommended while taking PROCYSBI (see Section 8.3 of the full prescribing information).**
- **Pediatric Use: The risks and benefits of treatment with PROCYSBI in children under 6 years old are not yet established (see Section 8.4 of the full prescribing information).**

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Researcher to Describe Role of Stem Cells in Diabetes

Douglas A. Melton

Stem cells offer hope for treatment of a host of diseases, and diabetes could be one of the most important. The potential of "Stem Cells to Understand and Treat Diabetes" will be the subject of a state-of-the-art lecture by Douglas A. Melton, PhD, on Thursday, Nov. 13.

Dr. Melton is the Saris University Professor at Harvard. He is also an investigator at the Howard Hughes Medical Institute and co-chair of the department of stem cell and regenerative biology at the Harvard Stem Cell Institute. Dr. Melton's laboratory studies how cell differentiation is directed during development and the role of stem cells in tissue regeneration. The lab's particular focus is the study of the genes and cells that make pancreatic tissue with the goal of making pancreatic cells for transplantation into people with diabetes.

Dr. Melton earned his doctorate in molecular biology from Cambridge University in the U.K. He has been with Harvard since 1981, and he and his wife serve as co-masters of a residential house for about 450 Harvard College undergraduates.

The author or co-author of more than 170 scientific publications, he is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences. His many awards include the Lounsberry Medal from the National Academy of Sciences and the Joslin Medal from the Joslin Diabetes Center. In recognition of his advocacy for stem cell research, he was chosen as the *Scientific American* policy leader of the year in 2007. He has twice been named one of *Time* magazine's 100 most influential people in the world.

ABIM President to Speak on Luring in New Physicians

Richard J. Baron

The president of the American Board of Internal Medicine (ABIM) will deliver the Christopher R. Blagg, MD, Lectureship in Renal Disease and Public Policy on the topic "Opportunities and Challenges: Attracting the Next Generation" on Thursday, Nov. 13.

In addition to leading ABIM, Richard J. Baron, MD, also heads the ABIM Foundation in Philadelphia. ABIM is a certifying board that works with 250,000 physicians in 19 specialties—about one in four practicing physicians in the United States. Dr. Baron leads a staff of 200.

Previously, Dr. Baron served as group director of seamless care models at the Centers for Medicare and Medicaid Services (CMS) Innovation Center, where he led efforts related to accountable care organizations and primary care. Prior to his CMS appointment, he practiced general internal medicine and geriatrics in Philadelphia at a practice that has been a pioneer in the adoption of electronic health records in the small practice environment. Before joining the federal government, he also served on the board and a technology advisory committee of the National Quality Forum as well as on the standards committee of the National Committee for Quality Assurance.

Dr. Baron served as chief medical officer of Health Partners, a not-for-profit Medicaid HMO set up by four teaching hospitals in Philadelphia, from 1988 to 1996. He was the architect of a best practices program, funded by the Robert Wood Johnson Foundation and the Center for Health Care Strategies, in which he worked with Medicaid health plans around the country to improve the quality of care for their members. This program reached plans serving more than half of the Medicaid managed care population in the United States.

Dr. Baron co-chairs the Public Health–Health Care Collaboration Workgroup, which provides recommendations to the Centers for Disease Control and Prevention. He is also a member of the newly formed Commonwealth Fund advisory group on health care reform, which aims to improve outcomes and lower costs for high-need, high-cost patients and vulnerable, low-income populations.

Dr. Baron received his medical degree from Yale University. He completed house staff training at New York University-Bellevue Medical Center and served a three-year obligation in the National Health Service Corps in rural Tennessee.

ASN gratefully acknowledges the Northwest Kidney Centers and its contributors for support of the Christopher R. Blagg, MD, Lectureship in Renal Disease and Public Policy. ASN thanks its Public Policy Board and the Renal Physicians Association for assistance with this session.

Brenner Lectureship to Look at Glomerular Disease

Martin R. Pollak

A leading researcher into the genetic basis of kidney disease will deliver the Barry M. Brenner, MD, Endowed Lectureship on Thursday, Nov. 13. Martin R. Pollak, MD, will speak on "APOL1 and Glomerular Disease."

Dr. Pollak is the chief of the renal division at Beth Israel Deaconess Medical Center in Boston. He is also professor of medicine at Harvard Medical School and an associate member of the Broad Institute.

African-Americans are at disproportionate risk for nondiabetic kidney disease, and particularly focal and segmental glomerulosclerosis (FSGS). Most of this disparity is due to two variants of the APOL1 gene. Dr. Pollak's work has shown that two common coding variants in the APOL1 gene confer resistance to trypanosomiasis, or sleeping sickness, a serious disease in some regions of Africa. But the variants also confer a sevenfold to tenfold increased susceptibility to FSGS and hypertension-associated kidney disease. His laboratory is currently working to identify the mechanisms by which these mutations in the APOL1 gene lead to a greater propensity for kidney damage.

Dr. Pollak serves on the scientific advisory board of the NephCure Foundation and was on the FSGS task force of the National Institute of Diabetes and Digestive and Kidney Diseases. For ASN, he has chaired the genetic subcommittee and served as a member of the program committee and the basic science committee.

He has served as an editorial reviewer for the *Journal of Clinical Investigation; Nephrology, Dialysis, and Transplantation*; and the *American Journal of Nephrology*.

He has received a physician scientist award from the National Institutes of Health as well as an achievement award and the Marilyn Farquhar Award for Podocyte Biology from the NephCure Foundation.

Dr. Pollak attended medical school at New York University School of Medicine. He completed his internship and residency in internal medicine at Columbia-Presbyterian Medical Center. He completed a fellowship in nephrology at Brigham and Women's Hospital in Boston and postdoctoral training in genetics at Harvard Medical School. He was a member of the department of medicine at Brigham and Women's Hospital of Harvard before being named to his current position.

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

Molecular Mechanisms Expert to Describe Findings on Slowing Cyst Progression

Peter Igarashi

An expert on molecular mechanisms underlying kidney function will deliver the Robert W. Schrier, MD, Endowed Lectureship on the topic "MicroRNAs that Slow Cyst Progression" on Thursday, Nov. 13.

Peter Igarashi, MD, FASN, is professor of internal medicine and pediatrics at the University of Texas Southwestern Medical Center in Dallas, where he holds the Robert Tucker Hayes Distinguished Chair in Nephrology. Dr. Igarashi is also director of the University of Texas Southwestern O'Brien Kidney Research Core Center.

Dr. Igarashi began his research career by investigating the molecular mechanisms underlying kidney-specific gene expression, which led to studies of transcriptional regulation of kidney development. He discovered the central role of the transcription factor HNF-1β in the expression of cystic disease genes and elucidated the molecular mechanisms by which mutations of HNF-1β produce kidney cysts and congenital kidney malformations.

His group has generated unique strains of mice that have been widely used for tissue-specific and inducible gene targeting in the kidney. In addition, Dr. Igarashi has studied the role of the primary cilium in the pathogenesis of polycystic kidney disease. His group was the first to demonstrate prospectively that the loss of the primary cilium was sufficient to produce kidney cysts. In related work, his laboratory has defined the relative contributions of bone marrow-derived stem cells and resident kidney cells in tubular regeneration following acute kidney injury. This work has led to Dr. Igarashi publishing more than 100 articles and book chapters.

Dr. Igarashi has served on the editorial boards of the *American Journal of Physiology-Renal Physiology* and *Journal of Clinical Investigation* as well as an associate editor of the *Journal of the American Society of Nephrology*. He has served on many study sections and grant review committees of the American Heart Association, National Kidney Foundation, and National Institutes of Health. Active in several national and international nephrology academic societies, he was the program chair of the 2008 ASN annual meeting.

Dr. Igarashi received an investigator award from the American Heart Association and a MERIT award from the National Institutes of Health.

Dr. Igarashi earned his MD degree from the University of California, Los Angeles, did his residency in internal medicine at the University of California, Davis Medical Center, and was a fellow in nephrology at the Yale University School of Medicine. He joined the faculty of Yale in 1987 and was recruited by the University of Texas Southwestern Medical Center in 1999.

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

Plenary Session

State-of-the-Art Lecture

DNA Expert to Lecture on Lessons from the Genetic Past

Eske Willerslev

An internationally recognized researcher in the fields of ancient DNA and evolutionary biology will unveil some secrets that can be learned from history in a state-of-the-art lecture entitled "What We Can Learn from the Genetic Past" on Friday, Nov. 14.

Eske Willerslev, DSc, is a professor at the University of Copenhagen in Denmark, where he is also director of the Centre of Excellence in GeoGenetics and the National CryoBank and Sequencing Facility. While completing his doctorate, Dr. Willerslev established the first ancient DNA facility in Denmark, which rapidly became internationally recognized for establishing the fields of ancient sedimentary and ice core genetics. He has participated in more than a dozen research field expeditions ranging from Greenland to northern Siberia to collect materials from megafauna fossils to glacier ice to ethnographic information.

Dr. Willerslev holds a full professorship at the University of Copenhagen as well as the prestigious position of visiting professor at Oxford University. His previous positions include professor of evolutionary biology and professor of ancient DNA at the Niels Bohr Institute at the University of Copenhagen. He has also been a fellow in the department of zoology at Oxford University and a research visitor at the M.D. Anderson Cancer Center at the University of Texas.

He has published 20 papers in *Science* and *Nature*, and 134 articles in other high-profile, peer-reviewed journals. He has been an invited speaker at 73 international conferences and been awarded 50 large research grants and academic prizes. He received an award in 2012 from the Danish Broadcasting Corporation for his efforts in communicating science to the public.

Coburn Lecture to Connect Bone, Muscle, and CKD

Mary B. Leonard

Mary B. Leonard, MD, will present the Jack W. Coburn, MD, Endowed Lectureship on Friday, Nov. 13. Dr. Leonard's topic will be "Frailty, Fractures, and the Bone-Muscle Connection in CKD."

Dr. Leonard is a professor of pediatrics and medicine at Stanford University School of Medicine. Her multidisciplinary research program is primarily focused on the detrimental effects of glucocorticoid therapy, muscle deficits, vitamin D deficiency, and inflammation on bone development in varied pediatric disorders. Her team uses novel imaging techniques to assess the unique effects of kidney disease on bone and muscle metabolism in children and adults. She has maintained continuous National Institutes of Health (NIH) funding for 17 years and serves as the primary mentor for many junior investigators supported by NIH awards.

She is a member of the Society of Pediatric Research and the American Society of Clinical Investigation. Dr. Leonard recently co-chaired the Kidney Disease: Improving Global Outcomes conference on controversies in chronic kidney disease and mineral and bone disorders. She is currently co-chairing the steering committee of a conference for developing positions on pediatric issues for the International Society of Clinical Densitometry.

She received a research fellowship from the National Kidney Foundation and a young investigator award from the American Society of Transplantation. She also received a faculty mentor award from the Children's Hospital of Philadelphia.

Before joining Stanford, Dr. Leonard was a professor of epidemiology and professor of pediatrics at the University of Pennsylvania School of Medicine. At the Children's Hospital of Pennsylvania, she was the director of clinical and translational research, director of research in the division of nephrology, and director of the pediatric nephrology fellowship program. She received her medical degree from Stanford University and her master's in clinical epidemiology from the University of Pennsylvania. She completed a residency in pediatrics, a fellowship in pediatric nephrology, and a fellowship in pediatric nutrition at the Children's Hospital of Philadelphia.

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

Winn Lecturer to Discuss Genetics of Glomerular Disease

Andrey S. Shaw

Andrey S. Shaw, MD, will deliver the Michelle P. Winn, MD, Endowed Lectureship on the genetics of human focal and segmental glomerulosclerosis (FSGS) on Friday, Nov. 14.

Dr. Shaw is the Emil R. Unanue Professor of Pathology and Immunology and head of the division of immunobiology at Washington University School of Medicine in St. Louis. He is also an investigator of the Howard Hughes Medical Institute.

Dr. Shaw is known for his contributions to our understanding of T cell signal transduction, protein kinases, and the role of podocytes in glomerular diseases. His interest in podocyte biology began with studies of knockout mice that lack a gene called CD2-associated protein, or CD2AP. Because data show that mutations in CD2AP can lead to human glomerular diseases such as FSGS, his team is using human genetics to define the epistatic network of genes involving CD2AP. FSGS is a disease of podocytes, so the team used bioinformatics to identify only those genes expressed in podocytes. They then selected 3000 genes they believed to be the likeliest epistatic candidates. Their goal is to sequence a set of kidney-specific genes in about 1000 FSGS patients and use statistical methods to analyze the pattern of rare variants in patients vs. controls to assemble a list of potential FSGS disease genes. The researchers expect these genes to be epistatic with CD2AP.

Dr. Shaw is the editor of *Molecular and Cellular Biology* and on the editorial board of *BMC Immunology*. He received a MERIT Award and a clinical investigator award from the National Institutes of Health and several distinguished service teaching awards from the medical school classes of Washington University.

He earned his bachelors and medical degrees from Columbia University and completed his residency in anatomic pathology and a postdoctoral fellowship at Yale University. He was an instructor at Yale before joining Washington University in 1991. He serves on the immunology program steering committee and the curriculum committee at Washington University Medical School.

ASN gratefully acknowledges Duke University School of Medicine, the school's Division of Nephrology, and several individuals for support of the Michelle P. Winn, MD, Endowed Lectureship.

Researcher to Receive Homer W. Smith Award

Friedhelm Hildebrandt

Acclaimed researcher Friedhelm Hildebrandt, MD, will receive the Homer W. Smith Award and deliver an address at Kidney Week on "Single-Gene Defects Elucidate Mechanisms of CKD."

Dr. Hildebrandt is the Warren E. Grupe Professor of Pediatrics at Harvard Medical School and chief of the division of nephrology at Boston Children's Hospital. He is also an investigator at the Howard Hughes Medical Institute.

The Homer W. Smith Award recognizes those who have made outstanding contributions to understanding how kidneys function in normal and diseased states, and Dr. Hildebrandt's research has increased this understanding in several areas.

His research is concerned with the identification and functional characterization of recessive single-gene causes of kidney diseases in children, including nephrotic syndrome, cystic renal ciliopathies, and congenital anomalies of the kidney. His group has identified more than 50 novel causative genes for chronic kidney disease and delineated the related pathogenesis.

Dr. Hildebrandt's lab studies the function of newly identified disease genes in disease models of mice and zebrafish as well as in cell-based systems. His work contributed to the early development of efficient methods for gene identification by combining homozygosity mapping with total human exome resequencing. His group recently discovered that DNA damage repair plays a role in the pathogenesis of ciliopathies.

His lab has also shown that in a very high percentage of cases of chronic kidney disease of childhood, a single gene may be identified using high-throughput sequencing techniques.

His lab's research has been supported solely by peer-reviewed research grants, mostly from the National Institutes of Health, the Howard Hughes Medical Institute, the Doris Duke Charitable Foundation, the March of Dimes, and the German Research Foundation. He has published more than 240 original articles.

Dr. Hildebrandt received his medical degree from Heidelberg University in Germany and his pediatric and nephrology training at Marburg University Children's Hospital. He was a postdoctoral research fellow at Yale University Medical School. He has received many awards, including the E. Mead Johnson Award from the Society for Pediatric Research, Franz Volhard Award from the German Society of Nephrology, and Lillian Jean Kaplan Award for Polycystic Kidney Disease Research. He is an elected member of the Association of American Physicians and the German National Academy of Sciences.

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.

Plenary Session

State-of-the-Art Lecture

Nanotechnology Expert to Describe Its Application to Medicine

Chad A. Mirkin

Smaller and smaller particles are doing bigger and bigger things in all fields of science. A specialist in these tiny matters will deliver a state-of-the-art lecture on "Realizing the Promise of Nanomedicine" on Saturday, Nov. 15.

A chemist and a world-renowned nanoscience expert, Chad A. Mirkin, PhD, is the director of the International Institute for Nanotechnology, the George B. Rathmann Professor of Chemistry, professor of chemical and biological engineering, professor of biomedical engineering, professor of materials science and engineering, and professor of medicine at Northwestern University in Evanston, Ill.

Dr. Mirkin's work has focused on developing methods for controlling the architecture of molecules and materials on the 1 nm to 100 nm length scale, and using them to develop novel analytical tools that can be applied in chemical and biological sensing, gene regulation, lithography, catalysis, optics, and energy generation, storage, and conversion. He has pioneered the use of biomolecules in materials science and the development of many nanoparticle-based extracellular and intracellular biodiagnostic and gene regulation tools.

This work has led to more than 560 publications and 243 patents, with several hundred more patent applications pending worldwide.

Dr. Mirkin has served on the editorial advisory boards of more than 20 scholarly journals, including *Biosensors & Bioelectronics, Biomacromolecules*, and *Macromolecular Bioscience*. He is an associate editor of the *Journal of the American Chemical Society* and the founding editor of the journal *Small*, one of the premier international nanotechnology journals.

Currently a member of the President's Council of Advisors on Science and Technology, he is the founder of three companies, Nanosphere, AuraSense, and AuraSense Therapeutics.

Dr. Mirkin's accomplishments have been recognized with more than 90 national and international awards, including the Linus Pauling Medal, the $500,000 Lemelson-MIT Prize, the Raymond and Beverly Sackler Prize in the Physical Sciences, the Feynman Prize in Nanotechnology, and the American Chemical Society Award for Creative Invention.

He is one of only 15 people to have been elected to all three U.S. national academies (Institute of Medicine, National Academy of Sciences, and National Academy of Engineering). He is also a fellow of the American Academy of Arts and Sciences.

Dr. Mirkin received his doctoral degree from Penn State. He was a National Science Foundation postdoc at the Massachusetts Institute of Technology prior to joining Northwestern in 1991.

Stuart L. Linas to be Given Robert G. Narins Award for Contributions in Education

Stuart L. Linas

Stuart L. Linas, MD, FASN, will receive the Robert G. Narins Award for his many contributions to medical education.

Dr. Linas is the Rocky Mountain Professor of Renal Research at the University of Colorado School of Medicine, where he has served on the faculty throughout his academic career. He has directed the renal fellowship program since 1984 and headed the section of hypertension within the division of renal diseases since 1994. He is also the chief of nephrology at Denver Health Medical Center.

Dr. Linas currently chairs the medical school's curriculum steering committee. He has won many teaching awards from medical students and house staff at the University of Colorado. Among these awards are the best teacher in third and fourth year clinical curriculum, an excellence in teaching award for the second year class, and the outstanding faculty award for house staff teaching. He also won the outstanding faculty teaching award from Denver Health.

Dr. Linas is treasurer of the American Board of Internal Medicine and is a past chair of its subspecialty board on nephrology. He has served ASN on the board of advisors, as the chair of the renal fellowship program directors committee and the hypertension advisory group, and on the education committee. He has served as president of the Association of Specialty Professors and on the board of directors of the Alliance of Academic Internal Medicine.

He was associate editor of *Nutrition and High Blood Pressure Reviews*. He has also served on the editorial boards of the *Internal Yearbook of Nephrology; American Journal of Physiology: Renal, Fluid, & Electrolyte Physiology; American Journal of Kidney Diseases; American Journal of Nephrology*; and *Clinical Journal of the American Society of Nephrology*.

After earning a medical degree from Tufts University School of Medicine, he completed his internal medicine residency at the University of Rochester School of Medicine and nephrology training at the University of Colorado.

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.

Congressional Champions of Kidney Patients to Receive President's Medal

Jim McDermott

Tom Marino

Two distinguished members of Congress will each receive a President's Medal for championing the cause of kidney patients and research in a special presentation during the plenary session on Saturday, Nov. 15.

Reps. Jim McDermott (D-Wash.) and Tom Marino (R-Pa.) are the co-chairs of the Congressional Kidney Caucus, which Rep. McDermott co-founded in 2002. The purpose of the bipartisan caucus is to educate members of Congress and the public about the problem kidney disease poses for society and the federal government's role in providing access to life-sustaining treatment for those with severe disease.

The two have deep personal interests in kidney conditions. Rep. Marino is a two-time survivor of kidney cancer. Rep. McDermott is not only a medical doctor, but he trained with his friend the legendary Belding Scribner in Seattle around the time that dialysis was invented.

As co-chairs of the Congressional Kidney Caucus, Reps. Marino and McDermott have raised awareness of kidney disease and the importance of increased investment in kidney research on Capitol Hill. They provided crucial early support for the Kidney Health Initiative and served as honorary co-hosts of several ASN congressional briefings on kidney disease research. They supported home dialysis patients by encouraging the secretary of health and human services to update training payments for home dialysis and by requesting a Government Accountability Office (GAO) report on the key factors that affect home dialysis use. They also agreed to partner in ASN's efforts to request a GAO report assessing the adequacy of the federal investment in combating kidney disease.

When he joined the Congressional Kidney Caucus, Rep. Marino said: "By sharing my personal experiences with other members of Congress, we will increase the awareness and understanding of the circumstances that face millions of Americans who suffer from kidney disease." He also co-chairs the Cystic Fibrosis Caucus and the Congressional Caucus on Foster Youth.

Rep. Marino first ran for Congress in 2010, winning a three-way Republican primary and then defeating a two-term Democratic incumbent by ten percentage points. Prior to entering politics, he worked in manufacturing. When he was passed over for a promotion, he realized the importance of a college degree, so at 30 years old he enrolled in college. He earned his bachelor's and law degrees in five year.

He practiced law for several years before being elected to two terms as Lycoming County district attorney. He later served as U.S. attorney for the middle district of Pennsylvania.

After completing his medical training, Rep. McDermott joined the U.S. Navy and was assigned to Long Beach Naval Station. He then moved to Seattle to pursue his specialty in psychiatry at the University of Washington Medical Center. He was soon elected to the state legislature, and he split his time to continue to practice medicine.

He served as a medical officer in the U.S. Foreign Service in 1987, and was assigned to Zaire. He returned home to run for the U.S. congressional seat representing the Seattle area in 1988, and is now serving his twelfth term. He is a senior member of the House Ways and Means Committee, which enables him to play an influential role in a wide range of issues, including Medicare.

Rep. McDermott supports the establishment of a single-payer healthcare system, and is working to increase the number of primary care doctors and decrease the costs of high-quality health care.

Plenary Session

John Peters Award to Honor Josephine P. Briggs

Josephine P. Briggs

ASN will recognize the wide-ranging contributions of Josephine P. Briggs, MD, with the presentation of the John P. Peters Award.

An accomplished researcher and physician, Dr. Briggs is director of the National Center for Complementary and Alternative Medicine at the National Institutes of Health (NIH).

The John P. Peters Award is given for outstanding contributions to improving the lives of patients and to furthering the understanding of the kidney in health and disease, and Dr. Briggs' research has added greatly to this understanding. In her current position, her focus on translational research is designed to bring a fuller understanding of the usefulness and safety of complementary and integrative health practices. She oversees an institute with a budget of $120 million that funds research at 260 institutions.

Dr. Briggs' research interests include the renin-angiotensin system, diabetic nephropathy, circadian regulation of blood pressure, and the effect of antioxidants in kidney disease. She has published more than 175 research articles, book chapters, and scholarly papers.

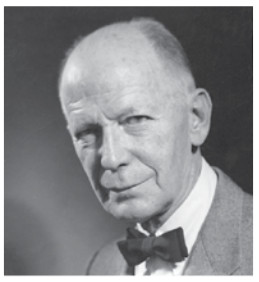
She has served on the editorial boards of several journals—including the *Journal of Laboratory and Clinical Medicine, Seminars in Nephrology,* and *Hypertension*—and was deputy editor of the *Journal of Clinical Investigation*.

After working as a research scientist for seven years at the Physiology Institute at the University of Munich in Germany, Dr. Briggs joined the faculty of the University of Michigan in 1985. She held several academic positions, including associate chair for research in the department of internal medicine and professorships in nephrology, internal medicine, and physiology.

Dr. Briggs joined the NIH in 1997 as director of the division of kidney, urologic, and hematologic diseases at the National Institute of Diabetes and Digestive and Kidney Diseases. While there, she co-chaired an NIH Roadmap Committee on Translational Core Resources. In 2006, she accepted a position as senior scientific officer at the Howard Hughes Medical Institute, and returned to NIH in 2008 for her present position.

She has received the Volhard Prize of the German Nephrological Society, Alexander von Humboldt Scientific Exchange Award, and NIH Director's awards. She is an elected member of the American Association of Physicians and the American Society of Clinical Investigation and a fellow of the American Association for the Advancement of Science. Dr. Briggs received her MD from Harvard Medical School and completed her residency in internal medicine and nephrology at the Mount Sinai School of Medicine in New York City.

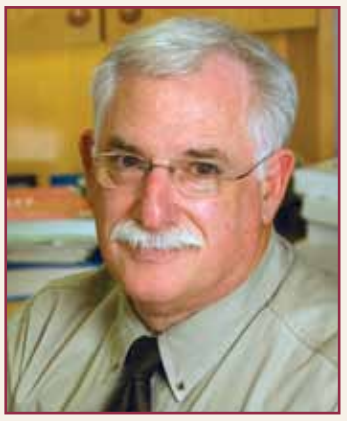
John P. Peters



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 Belding Scribner Award on Allan J. Collins



Allan J. Collins

The Belding H. Scribner Award will be tendered to Allan J. Collins, MD, for his career-long contributions to the practice of nephrology.

Dr. Collins is professor of medicine at the University of Minnesota School of Medicine and Hennepin County Medical Center and director of the Chronic Disease Research Group of the Minneapolis Medical Research Foundation.

Established in 1995, the Belding H. Scribner Award is presented to individuals who have made outstanding contributions to the care of patients with renal disorders or have substantially influenced the clinical practice of nephrology. Dr. Collins has made significant contributions in patient care, research, and service to professional organizations.

His clinical experience and research have focused on acute and chronic care of end stage renal disease patients and clinical studies of dialysis techniques and outcomes. He has also done extensive work with high-efficiency dialysis, the technical elements of dialysis, billing systems, and computer systems and operations.

The Chronic Disease Research Group was founded as Nephrology Analytical Services, but under Dr. Collins' leadership it has expanded beyond kidney disease to include other chronic conditions.

From 1983 to 1995, Dr. Collins managed the Metropolitan Dialysis Division and the clinical database of the Regional Kidney Disease Program at Hennepin County Medical Center, coordinating all areas of patient care, data collection, quality assurance, death reviews, computer systems, and analyses.

Dr. Collins has served the National Kidney Foundation in many capacities, including as president for three years. He has also been on the foundation's scientific advisory board and its kidney dialysis outcomes quality initiative. He served on the Commission for the Global Advancement of Nephrology Committee of the International Society of Nephrology.

Belding H. Scribner

Belding H. Scribner, MD, developed the arteriovenous shunt, which made possible long-term hemodialysis for chronic renal failure.

Dr. Scribner served as head of the University 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 dialysis 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.

ASN Scientific Exposition

Thursday, November 13 – Saturday, November 15

9:30 a.m. – 2:30 p.m.

Highlights Include:

- Over 150 Exhibiting Companies
- ASN Services
  - General Information, KHI, Membership Services, Publications, Foundation, and Web Services
- Career Fair
- Complimentary Refreshment Breaks
- Cyber Center
- Exhibitor Spotlights
- Innovators Place
- "Locate Me" Kiosks – Posters/Exhibitors
- Poster Sessions
- Wi-Fi

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 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 13

10:00 a.m. – 11:00 a.m.

Current Concepts in Secondary Hyperparathyroidism

Presented by AMGEN

12:30 p.m. – 1:30 p.m.

Advancing Paradigm Changes in Type 2 Diabetes Management

Presented by janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Friday, November 14

10:00 a.m. – 11:00 a.m.

Rituxan for the Treatment of GPA and MPA

Presented by Genentech | biogen idec

12:30 p.m. – 1:30 p.m.

Ferric Citrate: The Latest Advance in Iron Based Phosphate Management

Presented by KERYX BIOPHARMACEUTICALS, INC

Saturday, November 15

10:00 a.m. – 11:00 a.m.

The Science of Biosimilars

Presented by Hospira

12:30 p.m. – 1:30 p.m.

Fabry Disease: A Nephrology Perspective

Presented by genzyme A SANOFI COMPANY

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Plenary Session

State-of-the-Art Lecture

Address to Explore Relationship of Autophagy and Metabolic Disease

Beth C. Levine

"Autophagy and Metabolic Diseases" is the title of a state-of-the-art lecture to be presented by one of the founders of the autophagy field on Sunday, Nov. 16.

Beth C. Levine, MD, is the director of the Center for Autophagy Research and the Charles Cameron Sprague Distinguished Chair in Biomedical Science at the University of Texas Southwestern.

Dr. Levine's laboratory has made fundamental discoveries that have helped to open up a new field of biomedical research—the role of autophagy in human health and disease. Autophagy is an essential, homeostatic process by which cells break down their own components. Dr. Levine's laboratory identified the mammalian autophagy gene, *beclin 1*, and defined a role for it and the autophagy pathway in tumor suppression, antiviral immunity, development, cell death regulation, lifespan regulation, and exercise-induced metabolic effects.

For example, Dr. Levine demonstrated how *Akt*, a gene in the insulin-signaling pathway activated in many cancers, inhibits autophagy by inactivating *beclin 1*, allowing unregulated tumor cell growth. She has also shown that the epidermal growth factor receptor, which is expressed at abnormally high levels by many types of cancer cells, deactivates autophagy by binding the protein *beclin 1*, leading to increased rates of tumor growth and chemotherapy resistance in non-small cell lung cancer.

Dr. Levine joined the faculty at Columbia University College of Physicians and Surgeons as associate professor of medicine in 1993. In 2004, she became the Jay P. Sanford Professor and chief of the division of infectious diseases at the University of Texas Southwestern Medical Center. In 2011, she became the director of the newly created Center for Autophagy Research. She has been a Howard Hughes Medical Institute Investigator since 2008.

Dr. Levine is a member of the American Society for Clinical Investigation, the American Association of Physicians, and the National Academy of Sciences. She received the 2014 Stanley J. Korsmeyer Award from the American Society for Clinical Investigation as well as an award for outstanding research from the American Cancer Society.

She received her MD from Cornell University Medical College and completed her postdoctoral training in infectious diseases and viral pathogenesis at the Johns Hopkins University School of Medicine.

Young Investigator Recognized for Mineral Metabolism Research

Myles Wolf

The ASN-AHA Young Investigator Award will be presented to Myles Wolf, MD, MMSc, for his groundbreaking research on mineral metabolism. He will describe his recent findings in an address: "Mineral (Mal)Adaptation to Kidney Disease."

Dr. Wolf is the Margaret Gray Morton Professor of Medicine at the Feinberg School of Medicine at Northwestern University in Chicago. He is the founding director of the Center for Translational Metabolism and Health and director of the physician-scientist training program at Feinberg.

The focus of Dr. Wolf's research is disordered mineral metabolism across the spectrum of chronic kidney disease, including dialysis, kidney transplantation, and earlier stages. His primary contributions have been in the area of hormonal regulation of phosphate homeostasis. He helped to characterize the physiological role of fibroblast growth factor 23 in health and in chronic kidney disease, and the impact of elevated levels on adverse clinical outcomes.

He serves on the editorial boards of the *Journal of the American Society of Nephrology, Clinical Journal of the American Society of Nephrology*, and *Seminars in Nephrology*, and as editor of the mineral metabolism section of *Current Opinion in Nephrology and Hypertension*. Dr. Wolf has been invited to deliver numerous national and international lectures on his research, and he has received several teaching, mentoring, and research awards.

After serving on the faculty of Harvard Medical School for five years, Dr. Wolf moved to Florida and the University of Miami's Miller School of Medicine, where he eventually served as chief of the division of nephrology and hypertension, director of the clinical research center, and assistant dean for translational and clinical research. He joined the Feinberg School of Medicine in 2013.

Dr. Wolf received his medical degree from the State University of New York Downstate College of Medicine in Brooklyn. He completed internal medicine training at the Massachusetts General Hospital and a nephrology fellowship at the Massachusetts General Hospital and the Brigham and Women's Hospital in Boston. During his research fellowship training, Dr. Wolf obtained a master's of medical sciences in clinical and physiological investigation from Harvard Medical School.

Policy Update

ASN Responds to Medicare's Proposed ESRD Program Changes

By Mark Lukaszewski

Every year the Centers for Medicare & Medicaid Services (CMS) releases its proposed rule for the End-Stage Renal Disease (ESRD) Prospective Payment System (PPS) and Quality Incentive Program (QIP). The American Society of Nephrology (ASN) Quality Metrics Task Force and Public Policy Board thoroughly assessed the proposed rule for potential effects on patient care and access to dialysis treatment before ASN submitted feedback to CMS.

Evaluating the quality of care patients receive, as well as their access to dialysis services and medications, are of the utmost importance in a bundled payment system. This article highlights ASN's key recommendations to CMS outlined in the society's recent comment letter.

Proposed adjustment to the ESRD PPS

ASN was pleased CMS codified the Protecting Access to Medicare Act of 2014 (PAMA) in the proposed rule, which will greatly mitigate the 10 percent cut to bundled payments Congress outlined in the American Taxpayer Relief Act. The PAMA provisions will help alleviate concerns raised by ASN and other stakeholders in the kidney community about the cut's potential effects on patient access to high-quality care, particularly in rural and inner-city areas.

Eliminating barriers to home dialysis use

Deciding which dialysis modality to use for their treatment is one of the most important decisions a patient will make. This is why ASN supports efforts to 1) ensure patients have access to their preferred treatment modality, and 2) help remove barriers that could discourage patients from pursuing certain modalities, including home dialysis.

ASN has always agreed with CMS' and Congress' stated goal of increasing home dialysis utilization in the United States. However, ASN was disappointed that in the proposed rule, CMS states that modality choice does not constitute medical justification for paying for more frequent hemodialysis treatments. Given that approximately 10 percent of patients in the United States receive dialysis at home and less than 2 percent of patients receive home hemodialysis, ASN believes that CMS should not preclude modality choice as a medical justification for more frequent hemodialysis treatments, as it could potentially have material adverse effects on patients' physical and emotional well-being.

ESRD QIP modifications

ASN provided CMS detailed guidance on the QIP and the proposed new, revised, or eliminated measures. The society emphasized that CMS should work transparently and collaboratively with the kidney community in measure development and specifications. Furthermore, ASN called for a conservative approach to the QIP and other grading systems. Specifically, CMS should focus on developing and implementing fewer measures that focus on the most meaningful items for patient care, rather than diluting the QIP and distracting dialysis providers with numerous measures of less substantial importance.

Pharmaceuticals and clarifying third-party medication distribution

Some pharmacies that distribute Medicare Part D medications have been inappropriately refusing to cover certain oral medications that are not prescribed for the treatment of renal dialysis services.

Currently, only medications directly related and essential to the provision of renal dialysis services should be paid for under the ESRD PPS. However, some Part D plans have refused to cover these medications or have required a prior authorization (which can take hours or days) before authorizing dispensing of medically necessary drugs not related to ESRD care. This is particularly concerning for time-sensitive medications like antibiotics, the oral versions of which are most often used to treat respiratory, urinary tract, or other infections not related to dialysis. In some instances, patients have required hospitalization or sought treatment in emergency departments in order to receive medications unrelated to maintenance dialysis. This is a complex issue and ASN is dedicated to continue working with CMS to guarantee that patients have access to necessary medications.

Implementing a risk-standardized 30-day all-cause hospital readmissions measure

ASN has strongly supported a standardized readmission ratio (SRR) measure in concept, and believes it could be an important indicator of patient care. However, the society is unable to support the currently proposed measure and it continues to urge CMS to work collaboratively and transparently with stakeholders to develop the optimal SRR measure for inclusion in the QIP. One major area of concern is if a discharged patient is readmitted prior to being seen at the dialysis facility, the facility is penalized even though it would not have the opportunity to intervene to possibly prevent the readmission.

ASN also encouraged CMS to clarify how unsuccessful kidney transplants would be addressed in this measure in the 6 months following the transplant. If a patient experiences graft rejection, it should not be reflected on the dialysis facility. These incidents reflect the transplant (and transplant complications) and therefore these patients and readmissions should be excluded. ASN is hopeful that in the future a well-defined SRR measure could have a positive effect on patient outcomes and looks forward to working with others in the community in order to make sure the SRR measure is focused for dialysis care.

Final implementation

CMS will likely release the final rule in early November, and ASN—with other kidney community stakeholders—will continue to advocate to CMS and Congress until then. For more information about the ESRD PPS and QIP or to read ASN's full comment letter, please visit ASN's advocacy website at http://www.asn-online.org/policy/webdocs/asn.pdf.

ASN Key Recommendations to CMS*

- Work transparently and collaboratively in measure development and specifications.
- Aim for parsimony in the QIP and other grading systems. Specifically, developing and implementing fewer measures that focus on the most meaningful items for patient care is a far better strategy than diluting both the QIP and the attention of dialysis providers with numerous measures of less substantial importance.
- Monitor the effects of the PPS on access to care, including the ability of ESRD beneficiaries to obtain promptly prescribed oral medications covered under Medicare Part D.
- Delay implementation of the SRR measure to the QIP until several serious concerns with the measure have been addressed.

*CMS = Centers for Medicare & Medicaid Services; ESRD = End-Stage Renal Disease; PPS = Prospective Payment System; QIP = Quality Incentive Program; SRR = standardized readmission ratio.

A Novel Ligand Trap Derived From the ActRIIA Receptor, Sotatercept, Is Being Investigated for Effects on Complications of CKD

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Chief Medical Officer
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An Overview of the TGF-β Superfamily

The transforming growth factor-β (TGF-β) superfamily is a large group of signaling molecules involved in the regulation of many cellular processes.[1] Depending on the type and state of the cell, the actions of the TGF-β superfamily can have pleiotropic effects.[2] The ligands of the TGF-β superfamily include activins, TGF-βs, bone morphogenetic proteins (BMPs), and growth/differentiation factors (GDFs), which bind to heterodimeric receptors containing serine/threonine kinase domains, that upon activation interact with a group of transcription factors called Smads.[1] Examples of these receptors include activin receptor type IIA/B (ActRIIA/B) and the type I activin-like kinase (ALK) co-receptor.[1] Ligand binding initiates receptor-mediated activation of a Smad complex, which translocates to the nucleus where it binds to DNA to activate gene expression (Fig. 1A).[1] The large variety of ligands, receptors, and Smad molecules of the TGF-β superfamily signaling system allows for diverse cellular influences.[1]

The TGF-β Superfamily as a Therapeutic Target for Chronic Kidney Disease

In chronic kidney disease (CKD), erythropoiesis and bone metabolism are perturbed and contribute to the development of anemia and mineral and bone disorder (CKD-MBD), which are associated with increased cardiovascular risk and mortality.[3-7] Members of the TGF-β superfamily have been studied as potential regulators of erythropoiesis and bone metabolism. Activin A was initially described as erythroid differentiation factor.[8] However, the mechanism by which activin A influences erythropoiesis remains unclear.[8] In fact, there are data from in vitro and in vivo studies that support both erythropoiesis-stimulatory and erythropoiesis-inhibitory effects.[9-12] The TGF-β superfamily has also been implicated in bone metabolism.[13] Activin A is one of the most abundant TGF-β superfamily member proteins found in bone.[14] Inhibin, an inhibitor of activin A produced in the ovaries, stimulates bone growth, and decreased inhibin expression is associated with post-menopausal bone loss.[15] Given the evidence, the TGF-β superfamily serves as a potentially novel target for the treatment of anemia and bone and mineral diseases associated with CKD.[16]

Sotatercept (ACE-011) and RAP-011

Sotatercept (ACE-011) and its murine analog, RAP-011, are fusion proteins that inhibit signaling through ActRIIA.[16] Sotatercept is a recombinant human fusion protein comprising the extracellular domain of ActRIIA and the Fc domain of immunoglobulin G1.[17] Mechanistically, sotatercept acts as a ligand trap that binds TGF-β superfamily ligands including activin A and others.[16,17] Binding of sotatercept to ActRIIA ligands inhibits receptor-mediated activation of the Smad 2(3)/4 complex and modifies downstream gene transcription (Fig. 1B).[14,17] The resulting effect is an overall inhibition of signaling cascades dependent on the activin receptor, which studies have shown to include erythropoiesis and bone metabolism.[14,17]

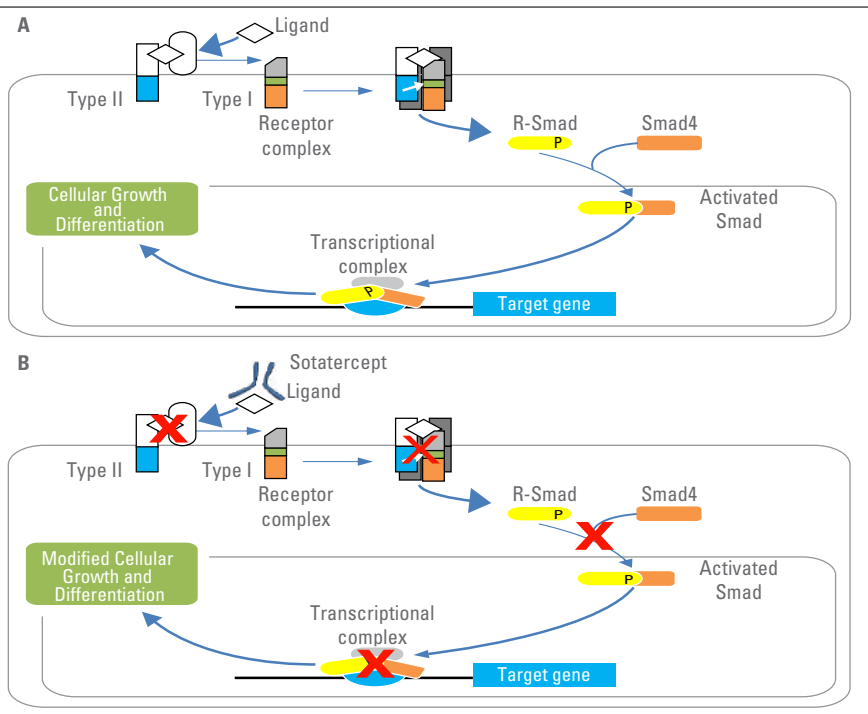

Figure 1. The TGF-β superfamily signaling system and the role of sotatercept.[1,17] A) Ligand binding initiates receptor-mediated activation of a transcriptional Smad complex, which translocates to the nucleus and acts as a transcription factor. Signaling may be dysregulated in certain disease states. B) Sotatercept traps ligands of the TGF-β superfamily, including activin A, to inhibit downstream pathways associated with ActRIIA signaling. This may improve regulation of cellular growth and differentiation in certain disease states. ActRIIA = activin receptor type IIA; ActRI = type I activin-like kinase receptor.

Potential Role for ActRIIA Signaling Inhibition in the Treatment of Anemia

Recent non-clinical studies suggest that RAP-011 may enhance erythropoiesis by blocking signaling through ActRIIA.[16,17]

- RAP-011 stimulates differentiation of mid-late erythroid precursors, distinguishing its role from that of erythropoietin (EPO)[17]
- RAP-011 may also act on BFU-E and indirectly on CFU-E through stimulation of EPO[17]
- Members of the TGF-β superfamily, such as GDF11 and activin A, may be negative growth regulators acting on late-stage erythropoiesis, and RAP-011 blocks these ligands to rapidly increase RBC parameters[17]
- Inhibition of ActRIIA signaling via RAP-011 stimulates RBC production, hemoglobin (Hb), and hematocrit (Hct) in healthy mice[17]
- In an established mouse model of CKD (5/6 nephrectomy) that exhibits anemia, 8 weeks of RAP-011 treatment significantly improved Hct values compared with control CKD mice treated with vehicle[16]

Potential Role for ActRIIA Signaling Inhibition in the Treatment of Bone Disease

Non-clinical studies suggest that RAP-011 modulates the imbalance between bone formation and bone resorption activity by blocking signaling through the ActRIIA receptor.[14,16,18-20]

- Activin A has been shown to stimulate the formation of osteoclasts in bone marrow–derived cultures and to inhibit the effects on osteoblasts[19,20]
- RAP-011 rescued the inhibitory effect of activin A on osteoblast function[18]
- In ovariectomized mice with established bone loss, RAP-011 promoted increases in bone mass and strength at multiple skeletal sites[14]
- In an established mouse model of CKD (5/6 nephrectomy) that exhibits bone loss, cortical bone thickness and bone volume/trabecular volume values significantly improved with 8 weeks of RAP-011 in comparison to control mice (Fig. 2)[16]

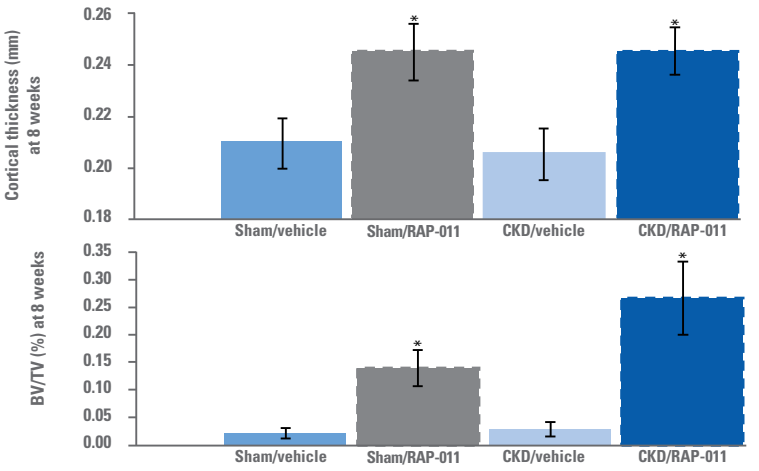

Figure 2. Impact of ActRIIA inhibition on bone parameters in CKD mouse model.[16] In the 5/6 nephrectomy model of CKD, 8 weeks of RAP-011 treatment significantly improved cortical thickness and bone volume/trabecular volume (BV/TV) values compared to vehicle control. The same effect was observed in the sham surgery controls in that RAP-011 treatment also exhibited improvements compared to vehicle control treatment.
*$P<0.05$ vs respective vehicle.

Sotatercept in ESKD patients

Given the potential role of ActRIIA signaling inhibition in the treatment of anemia and bone disease, sotatercept's impact on end-stage kidney disease (ESKD) is being investigated.[16,21,22] ACE-011-REN-001 is a 2-part, Phase 2A, randomized, placebo-controlled trial of sotatercept evaluating the pharmacokinetics, safety, tolerability, and efficacy on Hb in ESKD patients receiving hemodialysis.[16,21,22] Part 2 is ongoing and designed as a multiple ascending-dose trial. Data from this study have been presented previously.[16,21-23]

Additionally, ACE-011-REN-002 is a 2-part, Phase 2, multicenter, randomized, open-label, multiple-dose study of intravenous and subcutaneous administration of sotatercept in patients with ESKD on hemodialysis switched from EPO-stimulating agents with staggered dose group escalation in Part 1.[24] Part 1 is ongoing.[24] This will be followed by Part 2, a parallel-group, active-controlled study of selected dose(s) and regimen(s) to evaluate the pharmacokinetics, safety, tolerability, efficacy, dosing regimen, and pharmacodynamics of sotatercept.[24]

Effects of sotatercept on bone turnover, bone mass, and vascular calcification are currently under investigation in both studies.[16]

Summary

Sotatercept inhibits signaling through the ActRIIA receptor and may have novel effects on complications of CKD, including anemia and CKD-MBD.[16] Based on in vitro, in vivo, and clinical data, inhibition of ActRIIA signaling using sotatercept or RAP-011 increases red blood cell parameters and increases bone mass.[14,16,19,20] At ASN Kidney Week 2014, new data will be presented on the effects of RAP-011 in a mouse model of vascular calcification, along with clinical data for sotatercept in ESKD patients from ACE-011-REN-001 for safety and tolerability results, blood pressure and hemoglobin measurements, as well as initial exploratory effects on CKD-MBD. These preliminary results encourage us to continue to study sotatercept in the ESKD population.

If you are interested in participating in sotatercept clinical trials in ESKD, please contact Daniel Aversa at (U.S.) +1-732-652-5671, daversa@celgene.com; or Yemisi Coker (Switzerland) +41-32-729-8759, ycoker@celgene.com.

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Dialysate Cooling May Help Protect Against Brain Damage

Hemodialysis can cause significant circulatory stress that negatively affects various organs, including the heart and brain. New research indicates that cooling dialysis fluids can protect against blood pressure changes that damage the brain. The findings, published in the *Journal of the American Society of Nephrology*, offer a simple and inexpensive way to improve dialysis care.

"This study demonstrates that paying attention to improving the tolerability of dialysis treatment—in this case by the simple and safe intervention of reducing the temperature of dialysate—does not just make patients feel better, but also can completely protect the brain from progressive damage," said senior author Christopher McIntyre, DM.

Through their investigations into the adverse consequences of hemodialysis treatment, McIntyre and his team noted that circulatory effects of hemodialysis are likely caused by hemodynamic factors that lead to perfusion anomalies in vulnerable vascular beds.

Their previous work demonstrated a link between hemodialysis and significant reductions in myocardial blood flow. Through a systematic review of the literature, they found that reducing the temperature of the dialysate is an effective intervention to reduce the frequency of intradialytic hypotension and does not adversely affect dialysis adequacy (Selby NM, McIntyre CW. *Nephrol Dial Transplant 2006*; 21(7):1883–1898). Intradialytic hypotension occurred 7.1 times less frequently with cool dialysis, and average post-dialysis arterial pressure was higher with cool-temperature dialysis by 11.3 mm Hg. None of the studies reviewed reported that cool dialysis led to a reduction in dialysis adequacy as assessed by urea clearance.

In this latest work, McIntyre and his colleagues looked to see if dialysate cooling might also have measurable beneficial effects on the brain. McIntyre was at the University of Nottingham in the UK while conducting this work but is now at the University of Western Ontario and the London Health Sciences Centre, in Canada. He noted that cognitive, psychological, and functional difficulties are present in many hemodialysis patients, with some experiencing deficiencies in memory, executive function, and language.

The team sought to characterize hemodialysis-induced brain injury by studying the effects of the treatment on brain white matter microstructure, as well as to determine whether dialysate cooling could provide protection against hemodialysis-associated brain injury. The researchers randomized 73 incident hemodialysis patients starting within 6 months to dialyze with a dialysate temperature of either 37° C or 0.5° C below the core body temperature. Patients were followed for one year.

Diffusion tensor magnetic resonance imaging tests revealed that hemodialysis patients exhibited a pattern of brain injury similar to that described in acute ischemic stroke: increased fractional anisotropy and reduced radial diffusivity. Therefore, hemodialysis patients may be susceptible to recurrent acute ischemic brain insults due to dialysis-induced circulatory stress, analogous to that observed previously in the muscular tissue of the heart.

"This is the first study to show that hemodialysis drives progressive white matter brain injury, and that the extent of this is proportional to the degree of dialysis-induced blood pressure instability," McIntyre said. "This provides a plausible biological basis for cognitive dysfunction, increasing dependency, and potentially depression."

The researchers found that simply dialyzing at 0.5° C below core body temperature completely protected against white matter changes at one year. No patients withdrew from the study owing to lack of treatment tolerability, and absolute brain protection was evident even when applying the most sensitive measures of detecting injury.

McIntyre noted that the study was limited to patients new to dialysis. He said it is unclear if the protective effects would also be seen in patients who have been receiving dialysis long-term and who may already be experiencing cognitive and other difficulties. Also, the study was relatively small in size and needs to be followed up by larger and longer studies to accurately assess the impact of this approach.

"The paper significantly extends our knowledge on the advantages derived from reducing the dialysate temperature in patients during hemodialysis," said Fresenius Medical Care's Ciro Tetta, MD, who was not involved with the research. "Further studies will need to relate this protection on brain white matter changes to a lesser incidence of neurologic and psychiatric disorders in the hemodialysis population."

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Journal View

Urinary Sodium Doesn't Predict Kidney Failure Risk

For patients with nondiabetic chronic kidney disease (CKD), urinary sodium excretion rate is not associated with the long-term risk of kidney failure, reports a study in *Kidney International*.

The study used data from 840 patients, mean age 51.7 years, enrolled in the Modification of Diet and Renal Disease Study. Only 5 percent had a history of diabetes. Baseline 24-hour urinary sodium excretion was analyzed for association with the long-term risk of kidney failure and with a composite outcome of kidney failure or all-cause mortality. Exploratory analyses evaluated the possible effects of GFR, proteinuria, and angiotensin-converting enzyme inhibitor use on the relationship between urine sodium and kidney failure.

At a median 6 years' follow-up, 617 patients had experienced kidney failure, and 723 had met the composite outcome. The mean baseline 24-hour urinary sodium excretion was 3.46 g/day, with quartile means of 2.14, 2.05, 3.70, and 4.96 g/day. However, the primary analysis found no significant association between urine sodium level and either outcome. This was so when both the initial baseline 24-hour urinary sodium level and the cumulative mean time-dependent values were used.

Exploratory analysis suggested a significant interaction with baseline proteinuria. In a two-slope model, at urine sodium excretion of less than 3 g/day, higher urine sodium levels were associated with increased risk of kidney failure in individuals with baseline proteinuria less than 1 g/day. By contrast, individuals with baseline proteinuria of 1 g/day or higher were at lower risk of kidney failure. There was no interaction among individuals with urine sodium of 3 g/day or higher.

The current guidelines recommend sodium intake of less than 2 g/day for patients with CKD; yet there are few data showing that sodium intake affects long-term outcomes. The new study shows no difference in kidney failure risk by urinary sodium excretion level in a population of patients with mainly nondiabetic CKD. Further study is needed to confirm the possible interaction with proteinuria [Fan L, et al. Urinary sodium excretion and kidney failure in nondiabetic chronic kidney disease. *Kidney Int* 2014; 86:582–586].

Dietary Acid Load Linked to CKD Risk Factors

Higher dietary acid load is associated with albuminuria and other risk factors for chronic kidney disease (CKD), according to a report in *BMC Nephrology*.

The study included data from 12,293 adults participating in National Health and Nutrition Examination Surveys between 1999 and 2004. Diet-dependent acid load was assessed in terms of estimated net acid excretion (NAEes), based on nutrient intake and body surface area. Associations of NAEes with advanced stages of CKD, albuminuria, and sociodemographic and clinical characteristics were assessed.

Among adults aged 40 to 60 years, poverty, black race, and male sex were all associated with higher NAEes levels. Individuals with higher NAEes were more likely to have albuminuria than were those with lower levels: odds ratio 1.57. There was also a trend toward an increased risk of decreased estimated GFR among individuals with higher NAEes, which remained significant after adjustment for confounders.

Dietary factors can affect acid-base status, and they have a significant impact on the course and progression of CKD. These population-based data show that higher NAEes levels are associated with albuminuria and low eGFR in adults in the United States.

High dietary acid load is also associated with sociodemographic risk factors for CKD. The authors suggest the possibility of interventions to reduce dietary acid load in populations at high risk for CKD [Banerjee T, et al. Dietary acid load and chronic kidney disease among adults in the United States. *BMC Nephrol* 2014; 15:137].

Continued on page 34

Journal View

New Combination Improves Heart Failure Outcomes

A new product combining an angiotensin-receptor blocker (ARB) and a neprilysin inhibitor lowers mortality and hospitalization rates in patients with heart failure, compared with enalapril, concludes a trial in the *New England Journal of Medicine*.

The PARADIGM-HF trial enrolled 8442 patients with class II, III, or IV heart failure and an ejection fraction of 40 percent or less. The patients were randomly assigned to treatment with LCZ696, consisting of the neprilysin inhibitor sacubitril and the ARB valsartan, 200 mg twice daily, or the angiotensin-converting enzyme inhibitor enalapril, 10 mg twice daily. Study medications were given in addition to recommended therapy. The main outcome of interest was a composite of cardiovascular death and heart failure hospitalization.

The study was halted early at a median follow-up time of 27 months, with evidence of "overwhelming benefit" in the LCZ696 group. The rates of the primary outcome were 21.8 percent with LCZ696 versus 26.5 percent with enalapril: hazard ratio (HR) 0.80 in the LCZ696 group.

All-cause mortality was 17.0 percent with LCZ696 and 19.8 percent with placebo, HR 0.84. The rates of death resulting from cardiovascular causes were 13.3 percent and 16.5 percent, respectively, HR 0.80. Treatment with LCZ696 was also associated with a reduced risk of heart failure hospitalization, HR 0.79. There was also significant improvement in heart failure–related symptoms and physical limitations, with about a 1-point difference in clinical summary score on the Kansas City Cardiomyopathy Questionnaire. LCZ696 was associated with higher rates of hypotension and nonserious angioedema but with lower rates of renal impairment, hyperkalemia, and cough.

Naprilysin inhibition increases levels of endogenous vasoactive peptides, counteracting the adverse effects of neurohormonal overactivation. The new study shows significant improvement in morbidity and mortality with LCZ696 in patients with heart failure and reduced ejection fraction, compared with enalapril. The PARADIGM-HF study "provides strong evidence that combined inhibition of the angiotensin receptor and neprilysin is superior to inhibition of the renin-angiotensin system alone in patients with chronic heart failure," the investigators conclude [McMurray JJ, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med* 2014: 371:993–1004].

Good Outcomes with Blood Pressure Self-Management Program

For primary care patients with hypertension and cardiovascular risk factors, a blood pressure self-monitoring intervention—including self-titration of medications—yields greater reductions in systolic blood pressure at 1 year, concludes a randomized trial in the *Journal of the American Medical Association*.

The Targets and Self-Management for the Control of Blood Pressure in Stroke and at Risk Groups (TASMIN-SR) trial included 552 patients with hypertension, baseline blood pressure 130/80 mm Hg or higher, and a history of stroke, coronary heart disease, diabetes, or chronic kidney disease. The patients were drawn from 59 primary care practices in the United Kingdom. One group received a self-management intervention, in which they self-monitored blood pressure and adjusted their medications according to an individualized self-titration algorithm. The blood pressure targets in the self-management group were office measurements of 130/80 mm Hg and home measurements of 120/75 mm Hg.

The control patients received usual care, with office-based blood pressure measurements and medication changes. Information on changes in blood pressure at 12 months' follow-up were available in 450 patients.

Blood pressure decreased from 143.1/80.5 mm Hg to 128.2/73.8 mm Hg in the self-management group versus 143.6/79.5 mm Hg to 137.8/76.3 mm Hg in the control group. After correction for baseline values, the study intervention was associated with a reduction of 9.2/3.4 mm Hg in blood pressure. With multiple imputation for missing values, the difference was 8.8/3.1 mm Hg.

The intervention yielded comparable reductions in blood pressure across patient subgroups, and adverse events were similar between the intervention and control groups. Patients in the self-management group had greater increases in antihypertensive drug prescriptions, particularly for calcium channel blockers and thiazides.

A previous trial showed good reductions in systolic blood pressure with self-monitoring and self-titration, but that study included few patients with cardiovascular disease or other high-risk conditions. The TASMIN-SR trial shows a significant 1-year reduction in systolic blood pressure with the self-management approach in hypertensive patients at high risk of cardiovascular events. Blood pressure self-monitoring with self-titration "is feasible and achievable in a high-risk population without special equipment and by following a modest amount of training and additional family physician input," the researchers write [McManus RJ, et al. Effect of self-monitoring and medication self-titration on systolic blood pressure in hypertensive patients at high risk of cardiovascular disease: the TASMIN-SR randomized clinical trial. *JAMA* 2014; 312:799–808].

What's Behind Rising Rates of Obstetric Renal Failure?

Recent increases in obstetric acute renal failure are limited to women with hypertensive disorders of pregnancy, suggests a report in the *British Medical Journal*.

The retrospective analysis included nearly 2.2 million hospital deliveries in Canada, excluding Quebec, between 2003 and 2010. Based on ICD-10 codes, the rate of obstetric acute renal failure increased by 61 percent during this period: from 1.66 per 10,000 deliveries in 2003 to 2004 to 2.68 per 10,000 in 2009 to 2010. There was also a 21 percent increase in the rate of postpartum hemorrhage, along with a slight increase in risk of hypertensive disorders of pregnancy. However, the temporal trend in renal failure remained significant after adjustment for these and other risk factors.

On further analysis, the increase in obstetric renal failure occurred exclusively in women with hypertensive disorders of pregnancy. This group showed an adjusted increase of 91 percent: from 15.6 to 28.8 per 10,000 deliveries. The trend was even more pronounced among women who had gestational hypertension with significant proteinuria: adjusted increase 171 percent. Of 58 excess cases of acute renal failure in 2009 to 2010, 47 were in women with hypertensive disorders of pregnancy and 42 in women with gestational hypertension and significant proteinuria.

In both the United States and Canada, the rates of obstetric acute renal failure have increased over the past decade. This large analysis of Canadian data suggests that this trend is limited to women with hypertensive disorders of pregnancy, with an even sharper increase in the smaller group of women with gestational hypertension and significant proteinuria. These trends raise the possibility that some aspect of preeclampsia management may be leading to an increased risk of obstetric acute renal failure [Mehrabadi A, et al. Hypertensive disorders of pregnancy and the recent increase in obstetric acute renal failure in Canada: population based retrospective cohort study. *BMJ* 2014; 349:g4731].

Atypical Antipsychotics Linked to AKI Risk

Older adults taking atypical antipsychotic drugs may be at increased risk of acute kidney injury (AKI), reports a study in the *Annals of Internal Medicine*.

Ontario health data were used to identify 97,777 adults aged 65 or older who received a new outpatient prescription for an oral atypical antipsychotic drug between 2003 and 2012. The drugs of interest were quetiapine, risperidone, and olanzapine. These patients were matched to the same number of control individuals with no such prescription. The rates of hospitalization for AKI, based on hospital diagnosis codes, within 90 days of the atypical antipsychotic prescription were compared between groups.

The patients prescribed atypical antipsychotics were at significantly increased risk of hospitalization with AKI: relative risk (RR) 1.73. The association remained significant in a subpopulation of patients with available data on serum creatinine levels: AKI risk was 5.46 versus 3.34 percent, for an absolute risk increase of 2.12 percent. Atypical antipsychotic drugs were also associated with an increased risk of hypotension, RR 1.91; acute urinary retention, RR 1.98; and all-cause mortality, RR 2.39.

Some adverse outcomes associated with atypical antipsychotic drugs, including hypotension, acute urinary retention, and the neuroleptic malignant syndrome or rhabdomyolysis, are known causes of AKI. These population-based data suggest an increased risk of AKI in older adults prescribed atypical antipsychotic drugs.

Atypical antipsychotic drugs are also linked to other adverse outcomes that might explain the increase in AKI. "The findings support current safety concerns about the use of these drugs in older adults," the investigators conclude [Hwang YJ, et al. Atypical antipsychotic drugs and the risk for acute kidney injury and other adverse outcomes in older adults: a population-based cohort study. *Ann Intern Med* 2014; 161:242–248].

ASN Kidney Week 2014

Educational Symposia Schedule

Thursday, November 13 – Saturday, November 15

Philadelphia Marriott Downtown

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.

Thursday, November 13 • 12:45 p.m. – 1:45 p.m.

Contemporary Paradigms in Hyperphosphatemia: Outcomes, Pathophysiology, and Management
Support for this symposium is provided by an educational grant from FRESENIUS MEDICAL CARE

Is the Future Now? Targeting the Podocyte in Membranous Nephropathy and FSGS
Support for this symposium is provided by an educational grant from Mallinckrodt Pharmaceuticals

Oral Iron Supplementation in CKD and Dialysis Patients: An Update
Support for this symposium is provided by an educational grant from KERYX BIOPHARMACEUTICALS, INC

SGLT2 Inhibitor Therapy in Patients with Mild to Moderate Diabetic Kidney Disease
Support for this symposium is provided by an educational grant from AstraZeneca

Friday, November 14 • 6:45 a.m. – 7:45 a.m.

Improving ESRD Patient Outcomes: What Can We Do Today—And What Should We Aim for Tomorrow?
This activity is supported by an educational donation provided by AMGEN

Treatment of Hyperuricemia in CKD
Support for this symposium is provided by an educational grant from
Takeda Pharmaceuticals International, Inc., U.S. Region

Friday, November 14 • 12:45 p.m. – 1:45 p.m.

A Review of Biosimilars and Their Role in Anemia Management
Support for this symposium is provided by an educational grant from Hospira

Basic Science Symposium—CRISPR/CAS: New Methods for Engineering the Genome
Sponsored by ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

Hyperkalemia: A Physiologic Approach to Diagnosis and Management
Support for this symposium is provided by an educational grant from AZS Pharma

PTH: Measurement and Meaning
This activity is supported by an educational donation provided by AMGEN

Taking the Decision to Heart: Which Phosphate Binder Is Best for My Patient?
Support for this symposium is provided by an educational grant from SANOFI RENAL

Saturday, November 15 • 12:45 p.m. – 1:45 p.m.

Anemia Management in Kidney Disease: Optimizing Treatment Response
This activity is supported by an educational donation provided by AMGEN

Fluid Management in Hemodialysis: What Does the Future Hold?
Support for this symposium is provided by an educational grant from FRESENIUS MEDICAL CARE

Relapse Prevention in ANCA-Associated Vasculitis: Current Therapy and Future Directions
Support for this symposium is provided by an educational grant from Genentech | biogen idec

Thrombotic Microangiopathy: Clinical Challenges
Support for this symposium is provided by an educational grant from ALEXION

ASN Foundation for Kidney Research

Time for a Cure

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

Established in 2012, the ASN Foundation for Kidney Research funds the Career Development Grants Program, the Ben J. Lipps Research Fellowship Program, the William and Sandra Bennett Clinical Scholars Program, and the Student Scholar Grants Program awarding over $3,000,000 annually to young investigators, fellows, nephrology educators, and medical students.

The ASN Foundation for Kidney Research congratulates the talented group of researchers and educators who were awarded grants in 2014.

Career Development Grants Program - Funding for New Investigators

Advancing the independent careers of young investigators in biomedical research, grants are awarded to applicants within seven years of their initial faculty appointment.

Carl W. Gottschalk Research Scholar Grants

Michael Butterworth, PhD
University of Pittsburgh
Aldosterone-Regulated MicroRNAs and Sodium Transport in the Distal Kidney Nephron

Kirk N. Campbell, MD
Ichan School of Medicine at Mount Sinai
Role of Dendrin in Glomerular Disease Progression

Krzysztof Kiryluk, MD
Columbia University
GWAS-based Pathogenesis Model of IgA Nephropathy

Timmy C. Lee, MD, FASN
University of Alabama at Birmingham
Natural History of Arteriovenous Fistula Maturation

Ethan P. Marin, MD, PhD
Yale School of Medicine
A Novel Mode of Vascular Function Regulation by Protein Palmitoylation

Brian B. Ratliff, PhD
New York Medical College
Posttranslational and Redox Modification Regulation of HMGB1 During Kidney Injury

Matthias Wolf, MD
University of Texas Southwestern Medical Center
The Role of Mucin 1 in Protection Against Nephrolithiasis by Regulation of the Renal Calcium Channel TRPV5

John Merrill Grant in Transplantation

Martin H. Oberbarnscheidt, MD, PhD
University of Pittsburgh
Intragraft Recipient Antigen Presenting Cells in Allograft Rejection

The NephCure Kidney International-ASN Foundation for Kidney Research Grant

Heon Yung Gee, MD, PhD
Boston Children's Hospital
Mutations in KANK2 and ARHGAP4 Cause Nephrotic Syndrome by Defects in RHO GTPase Signaling

Student Scholar Grants Program

The ASN Foundation for Kidney Research enables medical students with an interest in either basic or clinical research to spend time engaged in work on a kidney research project.

Nicholas Apostolopoulos
Yale University School of Medicine
An Investigation into Alternative M2 Macrophage Activation After Renal Ischemia/Reperfusion Injury

Beatriz M. Cole
Mount Sinai School of Medicine
KIBRA Signaling in Glomerular Disease

Alexander Cypro
Washington State University
Reliability of Diagnosis for AKI in the Administrative Record of Hospitalized Patients

Colin P. Dunn
Albert Einstein College of Medicine
De novo Sirolimus as Primary Immunosupression in Renal Transplantation: A Single Center Study

Raymond W. Keller, Jr.
Emory University School of Medicine
Effects of Uremia on Urea Transporter Expression in Rat Eccrine Glands and the Sweat: Blood Ratio of Urea, Sodium, and Potassium

Robyn Nicole Levine
University of North Carolina School of Medicine
The Relationship Between Health/Functional Literacy and Hospitalizations for Children, Adolescents and Young Adults with CKD

Christopher J. Loftus
Cleveland Clinic
Effect of Vitamin D Supplementation on Renal Stone Risk and Composition

George Maliha
University of Pennsylvania School of Medicine
VaSera Basic Study

Kailey Minnings
The Hospital for Sick Children
The Rivas 1000 Cohort Validation Study

Richard T. Rogers
Emory University
Urea Transport and Blood Pressure Regulation

Tyler J. Stephenson
University of Kansas Medical Center
Characterizing the Effects of Cardiotrophin-Like Cytokine Factor 1 on Differentiated Podocytes

Heywan M. Tesfaye
Keck School of Medicine of USC
Molecular Mechanisms Responsible for the Blood Pressure Lowering Effect of CYP4A1 Expression

Harry Philip Tseng
Albany Medical College
BK Virus Serostatus Effects on Viremia and Nephropathy Post Renal Transplantation

Ben J. Lipps Research Fellowship Program

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

Ben J. Lipps Research Fellows

Akinwande A. Akinfolarin, MBBS
Brigham and Women's Hospital
The Role of DNA Damage Mediators in Kidney Fibrosis Following Tubular Injury

Pei-Lun Chu, MD, PhD
University of Virginia
Defining the Role of Endothelial Collectrin in Blood Pressure Homeostasis

Daniel Fantus, MD
University of Pittsburgh Medical Center
Role of Mechanistic Target of Rapamycin (mTOR) Complexes in Regulation of Alloimmunity and Transplant Rejection

Silvia Ferrè, PhD
University of Texas Southwestern Medical Center
Understanding the Regulation of HNF-1 Beta Expression by ER Stress Effectors

Michelle M. O'Shaughnessy, MbChB
Stanford University School of Medicine
Trends in the Incidence, Clinical Characteristics, and Outcomes of Patients with End-Stage Renal Disease Due to Glomerulonephritis

Sharon Anderson Research Fellow

Moshe Shashar, MD
Boston Medical Center
Role of Uremic Solutes in Thrombosis

Joseph A. Carlucci Research Fellow

Gene-Yuan Chang, MD
University of California, San Francisco
Characterizing Renal Gluconeogenesis and its Regulation in Wild-Type, Insulin-Resistant and Diabetic Rats

Donald E. Wesson Research Fellow

Nicholas Zwang, MD
Massachusetts General Hospital
Pharmacologic Phosphatidylinositol-3 Kinase Inhibition in Regulatory T Cells

ASN Foundation for Kidney Research Fellows

Javier A. Neyra, MD
University of Texas Southwestern Medical Center
Klotho and Acute Kidney Injury: A Case-Control Study in Humans

Rabi Yacoub, MD
Ichan School of Medicine at Mount Sinai
Nephrin's Role in Maintaining an Intact Slit Diaphragm in Adult Mice

William and Sandra Bennett Clinical Scholars Program

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

Jane O. Schell, MD
University of Pittsburgh Medical Center
An Innovative Communication Curriculum Designed to Improve Nephrology Trainees' Knowledge and Skills in Discussing Advance Care Planning and End of Life

2014
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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.

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Index to Advertisers

SAMSCA® (tolvaptan) tablets for oral use

Brief Summary of Prescribing Information. Please see Full Prescribing Information for complete product information.

WARNING: INITIATE AND RE-INITIATE IN A HOSPITAL AND MONITOR SERUM SODIUM

SAMSCA should be initiated and re-initiated in patients only in a hospital where serum sodium can be monitored closely. Too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours) can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death. In susceptible patients, including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable.

INDICATIONS AND USAGE: SAMSCA is indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone (SIADH).

Important Limitations: Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with SAMSCA. It has not been established that raising serum sodium with SAMSCA provides a symptomatic benefit to patients.

CONTRAINDICATIONS: SAMSCA is contraindicated in the following conditions:

Urgent need to raise serum sodium acutely: SAMSCA has not been studied in a setting of urgent need to raise serum sodium acutely.

Inability of the patient to sense or appropriately respond to thirst: Patients who are unable to auto-regulate fluid balance are at substantially increased risk of incurring an overly rapid correction of serum sodium, hypernatremia and hypovolemia.

Hypovolemic hyponatremia: Risks associated with worsening hypovolemia, including complications such as hypotension and renal failure, outweigh possible benefits.

Concomitant use of strong CYP 3A inhibitors: Ketoconazole 200 mg administered with tolvaptan increased tolvaptan exposure by 5-fold. Larger doses would be expected to produce larger increases in tolvaptan exposure. There is not adequate experience to define the dose adjustment that would be needed to allow safe use of tolvaptan with strong CYP 3A inhibitors such as clarithromycin, ketoconazole, itraconazole, ritonavir, indinavir, nelfinavir, saquinavir, nefazodone, and telithromycin.

Anuric patients: In patients unable to make urine, no clinical benefit can be expected.

Hypersensitivity: SAMSCA is contraindicated in patients with hypersensitivity (e.g. anaphylactic shock, rash generalized) to tolvaptan or any component of the product *[see Adverse Reactions (6.2)]*.

WARNINGS AND PRECAUTIONS:

Too Rapid Correction of Serum Sodium Can Cause Serious Neurologic Sequelae (see BOXED WARNING): Osmotic demyelination syndrome is a risk associated with too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours). Osmotic demyelination results in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma or death. In susceptible patients including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable. In controlled clinical trials in which tolvaptan was administered in titrated doses starting at 15 mg once daily, 7% of tolvaptan-treated subjects with a serum sodium <130 mEq/L had an increase in serum sodium greater than 8 mEq/L at approximately 8 hours and 2% had an increase greater than 12 mEq/L at 24 hours. Approximately 1% of placebo-treated subjects with a serum sodium <130 mEq/L had a rise greater than 8 mEq/L at 8 hours and no patient had a rise greater than 12 mEq/L/24 hours. Osmotic demyelination syndrome has been reported in association with SAMSCA therapy *[see Adverse Reactions (6.2)]*. Patients treated with SAMSCA should be monitored to assess serum sodium concentrations and neurologic status, especially during initiation and after titration. Subjects with SIADH or very low baseline serum sodium concentrations may be at greater risk for too-rapid correction of serum sodium. In patients receiving SAMSCA who develop too rapid a rise in serum sodium, discontinue or interrupt treatment with SAMSCA and consider administration of hypotonic fluid. Fluid restriction during the first 24 hours of therapy with SAMSCA may increase the likelihood of overly-rapid correction of serum sodium, and should generally be avoided.

Liver Injury: SAMSCA can cause serious and potentially fatal liver injury. In a placebo-controlled and open label extension study of chronically administered tolvaptan in patients with autosomal dominant polycystic kidney disease, cases of serious liver injury attributed to tolvaptan were observed. An increased incidence of ALT greater than three times the upper limit of normal was associated with tolvaptan (42/958 or 4.4%) compared to placebo (5/484 or 1.0%). Cases of serious liver injury were generally observed starting 3 months after initiation of tolvaptan although elevations of ALT occurred prior to 3 months. Patients with symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice should discontinue treatment with SAMSCA. Limit duration of therapy with SAMSCA to 30 days. Avoid use in patients with underlying liver disease, including cirrhosis, because the ability to recover from liver injury may be impaired. *[see Adverse Reactions (6.1)]*.

Dehydration and Hypovolemia: SAMSCA therapy induces copious aquaresis, which is normally partially offset by fluid intake. Dehydration and hypovolemia can occur, especially in potentially volume-depleted patients receiving diuretics or those who are fluid restricted. In multiple-dose, placebo-controlled trials in which 607 hyponatremic patients were treated with tolvaptan, the incidence of dehydration was 3.3% for tolvaptan and 1.5% for placebo-treated patients. In patients receiving SAMSCA who develop medically significant signs or symptoms of hypovolemia, interrupt or discontinue SAMSCA therapy and provide supportive care with careful management of vital signs, fluid balance and electrolytes. Fluid restriction during therapy with SAMSCA may increase the risk of dehydration and hypovolemia. Patients receiving SAMSCA should continue ingestion of fluid in response to thirst.

Co-administration with Hypertonic Saline: Concomitant use with hypertonic saline is not recommended.

Drug Interactions:

Other Drugs Affecting Exposure to Tolvaptan:

CYP 3A Inhibitors: Tolvaptan is a substrate of CYP 3A. CYP 3A inhibitors can lead to a marked increase in tolvaptan concentrations *[see Dosage and Administration (2.3), Drug Interactions (7.1)]*.

Do not use SAMSCA with strong inhibitors of CYP 3A *[see Contraindications (4.4)]* and avoid concomitant use with moderate CYP 3A inhibitors.

CYP 3A Inducers: Avoid co-administration of CYP 3A inducers (e.g., rifampin, rifabutin, rifapentin, barbiturates, phenytoin, carbamazepine, St. John's Wort) with SAMSCA, as this can lead to a reduction in the plasma concentration of tolvaptan and decreased effectiveness of SAMSCA treatment. If co-administered with CYP 3A inducers, the dose of SAMSCA may need to be increased *[see Dosage and Administration (2.3), Drug Interactions (7.1)]*.

P-gp Inhibitors: The dose of SAMSCA may have to be reduced when SAMSCA is co-administered with P-gp inhibitors, e.g., cyclosporine *[see Dosage and Administration (2.3), Drug Interactions (7.1)]*.

Hyperkalemia or Drugs that Increase Serum Potassium: Treatment with tolvaptan is associated with an acute reduction of the extracellular fluid volume which could result in increased serum potassium. Serum potassium levels should be monitored after initiation of tolvaptan treatment in patients with a serum potassium >5 mEq/L as well as those who are receiving drugs known to increase serum potassium levels.

ADVERSE REACTIONS:

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse event information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates. In multiple-dose, placebo-controlled trials, 607 hyponatremic patients (serum sodium <135 mEq/L) were treated with SAMSCA. The mean age of these patients was 62 years; 70% of patients were male and 82% were Caucasian. One hundred eighty nine (189) tolvaptan-treated patients had a serum sodium <130 mEq/L, and 52 patients had a serum sodium <125 mEq/L. Hyponatremia was attributed to cirrhosis in 17% of patients, heart failure in 68% and SIADH/other in 16%. Of these patients, 223 were treated with the recommended dose titration (15 mg titrated to 60 mg as needed to raise serum sodium). Overall, over 4,000 patients have been treated with oral doses of tolvaptan in open-label or placebo-controlled clinical trials. Approximately 650 of these patients had hyponatremia; approximately 219 of these hyponatremic patients were treated with tolvaptan for 6 months or more. The most common adverse reactions (incidence ≥5% more than placebo) seen in two 30-day, double-blind, placebo-controlled hyponatremia trials in which tolvaptan was administered in titrated doses (15 mg to 60 mg once daily) were thirst, dry mouth, asthenia, constipation, pollakiuria or polyuria and hyperglycemia. In these trials, 10% (23/223) of tolvaptan-treated patients discontinued treatment because of an adverse event, compared to 12% (26/220) of placebo-treated patients; no adverse reaction resulting in discontinuation of trial medication occurred at an incidence of >1% in tolvaptan-treated patients.

Table 1 lists the adverse reactions reported in tolvaptan-treated patients with hyponatremia (serum sodium <135 mEq/L) and at a rate at least 2% greater than placebo-treated patients in two 30-day, double-blind, placebo-controlled trials. In these studies, 223 patients were exposed to tolvaptan (starting dose 15 mg, titrated to 30 and 60 mg as needed to raise serum sodium). Adverse events resulting in death in these trials were 6% in tolvaptan-treated-patients and 6% in placebo-treated patients.

Table 1. Adverse Reactions (>2% more than placebo) in Tolvaptan-Treated Patients in Double-Blind, Placebo-Controlled Hyponatremia Trials

System Organ Class MedDRA Preferred Term	Tolvaptan 15 mg/day-60 mg/day (N = 223) n (%)	Placebo (N = 220) n (%)
Gastrointestinal Disorders		
Dry mouth	28 (13)	9 (4)
Constipation	16 (7)	4 (2)
General Disorders and Administration Site Conditions		
Thirst[a]	35 (16)	11 (5)
Asthenia	19 (9)	9 (4)
Pyrexia	9 (4)	2 (1)
Metabolism and Nutrition Disorders		
Hyperglycemia[b]	14 (6)	2 (1)
Anorexia[c]	8 (4)	2 (1)
Renal and Urinary Disorders		
Pollakiuria or polyuria[d]	25 (11)	7 (3)

The following terms are subsumed under the referenced ADR in Table 1:

[a]polydipsia; [b]diabetes mellitus; [c]decreased appetite; [d]urine output increased, micturition, urgency, nocturia

In a subgroup of patients with hyponatremia (N = 475, serum sodium <135 mEq/L) enrolled in a double-blind, placebo-controlled trial (mean duration of treatment was 9 months) of patients with worsening heart failure, the following adverse reactions occurred in tolvaptan-treated patients at a rate at least 2% greater than placebo: mortality (42% tolvaptan, 38% placebo), nausea (21% tolvaptan, 16% placebo), thirst (12% tolvaptan, 2% placebo), dry mouth (7% tolvaptan, 2% placebo) and polyuria or pollakiuria (4% tolvaptan, 1% placebo).

Gastrointestinal bleeding in patients with cirrhosis: In patients with cirrhosis treated with tolvaptan in the hyponatremia trials, gastrointestinal bleeding was reported in 6 out of 63 (10%) tolvaptan-treated patients and 1 out of 57 (2%) placebo treated patients. The following adverse reactions occurred in <2% of hyponatremic patients treated with SAMSCA and at a rate greater than placebo in double-blind placebo-controlled trials (N = 607 tolvaptan; N = 518 placebo) or in <2% of patients in an uncontrolled trial of patients with hyponatremia (N = 111) and are not mentioned elsewhere in the label: *Blood and Lymphatic System Disorders: Disseminated intravascular coagulation; Cardiac Disorders: Intracardiac thrombus, ventricular fibrillation; Investigations: Prothrombin time prolonged; Gastrointestinal Disorders: Ischemic colitis; Metabolism and Nutrition Disorders: Diabetic ketoacidosis; Musculoskeletal and Connective Tissue Disorders: Rhabdomyolysis; Nervous System: Cerebrovascular accident; Renal and Urinary Disorders: Urethral hemorrhage; Reproductive System and Breast Disorders (female): Vaginal hemorrhage; Respiratory, Thoracic, and Mediastinal Disorders: Pulmonary embolism, respiratory failure; Vascular disorder: Deep vein thrombosis.*

Postmarketing Experience: The following adverse reactions have been identified during post-approval use of SAMSCA. Because these reactions are reported voluntarily from a population of an unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Neurologic: Osmotic demyelination syndrome; *Investigations:* Hypernatremia. Removal of excess free body water increases serum osmolality and serum sodium concentrations. All patients treated with tolvaptan, especially those whose serum sodium levels become normal, should continue to be monitored to ensure serum sodium remains within normal limits. If hypernatremia is observed, management may include dose decreases or interruption of tolvaptan treatment, combined with modification of free-water intake or infusion. During clinical trials of hyponatremic patients, hypernatremia was reported as an adverse event in 0.7% of patients receiving tolvaptan vs. 0.6% of patients receiving placebo; analysis of laboratory values demonstrated an incidence of hypernatremia of 1.7% in patients receiving tolvaptan vs. 0.8% in patients receiving placebo. *Immune System Disorders:* Hypersensitivity reactions including anaphylactic shock and rash generalized *[see Contraindications (4.6)]*.

DRUG INTERACTIONS:

Effects of Drugs on Tolvaptan:

Ketoconazole and Other Strong CYP 3A Inhibitors: SAMSCA is metabolized primarily by CYP 3A. Ketoconazole is a strong inhibitor of CYP 3A and also an inhibitor of P-gp. Co-administration of SAMSCA and ketoconazole 200 mg daily results in a 5-fold increase in exposure to tolvaptan. Co-administration of SAMSCA with 400 mg ketoconazole daily or with other strong CYP 3A inhibitors (e.g., clarithromycin, itraconazole, telithromycin, saquinavir, nelfinavir, ritonavir and nefazodone) at the highest labeled dose would be expected to cause an even greater increase in tolvaptan exposure. Thus, SAMSCA and strong CYP 3A inhibitors should not be co-administered *[see Dosage and Administration (2.3) and Contraindications (4.4)]*.

Moderate CYP 3A Inhibitors: The impact of moderate CYP 3A inhibitors (e.g., erythromycin, fluconazole, aprepitant, diltiazem and verapamil) on the exposure to co-administered tolvaptan has not been assessed. A substantial increase in the exposure to tolvaptan would be expected when SAMSCA is co-administered with moderate CYP 3A inhibitors. Co-administration of SAMSCA with moderate CYP3A inhibitors should therefore generally be avoided *[see Dosage and Administration (2.3) and Warnings and Precautions (5.5)]*. **Grapefruit Juice:** Co-administration of grapefruit juice and SAMSCA results in a 1.8-fold increase in exposure to tolvaptan *[see Dose and Administration (2.3) and Warnings and Precautions (5.5)]*. **P-gp Inhibitors:** Reduction in the dose of SAMSCA may be required in patients concomitantly treated with P-gp inhibitors, such as e.g., cyclosporine, based on clinical response *[see Dose and Administration (2.3) and Warnings and Precautions (5.5)]*. **Rifampin and Other CYP 3A Inducers:** Rifampin is an inducer of CYP 3A and P-gp. Co-administration of rifampin and SAMSCA reduces exposure to tolvaptan by 85%. Therefore, the expected clinical effects of SAMSCA in the presence of rifampin and other inducers (e.g., rifabutin, rifapentin, barbiturates, phenytoin, carbamazepine and St. John's Wort) may not be observed at the usual dose levels of SAMSCA. The dose of SAMSCA may have to be increased *[Dosage and Administration (2.3) and Warnings and Precautions (5.5)]*. **Lovastatin, Digoxin, Furosemide, and Hydrochlorothiazide:** Co-administration of lovastatin, digoxin, furosemide, and hydrochlorothiazide with SAMSCA has no clinically relevant impact on the exposure to tolvaptan.

Effects of Tolvaptan on Other Drugs: Digoxin: Digoxin is a P-gp substrate. Co-administration of SAMSCA with digoxin increased digoxin AUC by 20% and Cmax by 30%. **Warfarin, Amiodarone, Furosemide, and Hydrochlorothiazide:** Co-administration of tolvaptan does not appear to alter the pharmacokinetics of warfarin, furosemide, hydrochlorothiazide, or amiodarone (or its active metabolite, desethylamiodarone) to a clinically significant degree. **Lovastatin:** SAMSCA is a weak inhibitor of CYP 3A. Co-administration of lovastatin and SAMSCA increases the exposure to lovastatin and its active metabolite lovastatin-β hydroxyacid by factors of 1.4 and 1.3, respectively. This is not a clinically relevant change.

Pharmacodynamic Interactions: Tolvaptan produces a greater 24 hour urine volume/excretion rate than does furosemide or hydrochlorothiazide. Concomitant administration of tolvaptan with furosemide or hydrochlorothiazide results in a 24 hour urine volume/excretion rate that is similar to the rate after tolvaptan administration alone. Although specific interaction studies were not performed, in clinical studies tolvaptan was used concomitantly with beta-blockers, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and potassium sparing diuretics. Adverse reactions of hyperkalemia were approximately 1-2% higher when tolvaptan was administered with angiotensin receptor blockers, angiotensin converting enzyme inhibitors and potassium sparing diuretics compared to administration of these medications with placebo. Serum potassium levels should be monitored during concomitant drug therapy. As a V_2 receptor antagonist, tolvaptan may interfere with the V_2 agonist activity of desmopressin (dDAVP). In a male subject with mild Von Willebrand (vW) disease, intravenous infusion of dDAVP 2 hours after administration of oral tolvaptan did not produce the expected increases in vW Factor Antigen or Factor VIII activity. It is not recommended to administer SAMSCA with V_2 agonist.

USE IN SPECIFIC POPULATIONS: There is no need to adjust dose based on age, gender, race, or cardiac function *[see Clinical Pharmacology (12.3)]*.

Pregnancy: Pregnancy Category C. There are no adequate and well controlled studies of SAMSCA use in pregnant women. In animal studies, cleft palate, brachymelia, microphthalmia, skeletal malformations, decreased fetal weight, delayed fetal ossification, and embryo-fetal death occurred. SAMSCA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In embryo-fetal development studies, pregnant rats and rabbits received oral tolvaptan during organogenesis. Rats received 2 to 162 times the maximum recommended human dose (MRHD) of tolvaptan (on a body surface area basis). Reduced fetal weights and delayed fetal ossification occurred at 162 times the MRHD. Signs of maternal toxicity (reduction in body weight gain and food consumption) occurred at 16 and 162 times the MRHD. When pregnant rabbits received oral tolvaptan at 32 to 324 times the MRHD (on a body surface area basis), there were reductions in maternal body weight gain and food consumption at all doses, and increased abortions at the mid and high doses (about 97 and 324 times the MRHD). At 324 times the MRHD, there were increased rates of embryo-fetal death, fetal microphthalmia, open eyelids, cleft palate, brachymelia and skeletal malformations *[see Nonclinical Toxicology (13.3)]*.

Labor and Delivery: The effect of SAMSCA on labor and delivery in humans is unknown.

Nursing Mothers: It is not known whether SAMSCA is excreted into human milk. Tolvaptan is excreted into the milk of lactating rats. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants from SAMSCA, a decision should be made to discontinue nursing or SAMSCA, taking into consideration the importance of SAMSCA to the mother.

Pediatric Use: Safety and effectiveness of SAMSCA in pediatric patients have not been established.

Geriatric Use: Of the total number of hyponatremic subjects treated with SAMSCA in clinical studies, 42% were 65 and over, while 19% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Increasing age has no effect on tolvaptan plasma concentrations.

Use in Patients with Hepatic Impairment: Moderate and severe hepatic impairment do not affect exposure to tolvaptan to a clinically relevant extent. No dose adjustment of tolvaptan is necessary. Avoid use of tolvaptan in patients with underlying liver disease.

Use in Patients with Renal Impairment: No dose adjustment is necessary based on renal function. There are no clinical trial data in patients with CrCl <10 mL/min, and, because drug effects on serum sodium levels are likely lost at very low levels of renal function, use in patients with a CrCl <10 mL/min is not recommended. No benefit can be expected in patients who are anuric *[see Contraindications 4.5) and Clinical Pharmacology (12.3)]*.

Use in Patients with Congestive Heart Failure: The exposure to tolvaptan in patients with congestive heart failure is not clinically relevantly increased. No dose adjustment is necessary.

OVERDOSAGE: Single oral doses up to 480 mg and multiple doses up to 300 mg once daily for 5 days have been well tolerated in studies in healthy subjects. There is no specific antidote for tolvaptan intoxication. The signs and symptoms of an acute overdose can be anticipated to be those of excessive pharmacologic effect: a rise in serum sodium concentration, polyuria, thirst, and dehydration/hypovolemia. The oral LD50 of tolvaptan in rats and dogs is >2000 mg/kg. No mortality was observed in rats or dogs following single oral doses of 2000 mg/kg (maximum feasible dose). A single oral dose of 2000 mg/kg was lethal in mice, and symptoms of toxicity in affected mice included decreased locomotor activity, staggering gait, tremor and hypothermia.

If overdose occurs, estimation of the severity of poisoning is an important first step. A thorough history and details of overdose should be obtained, and a physical examination should be performed. The possibility of multiple drug involvement should be considered. Treatment should involve symptomatic and supportive care, with respiratory, ECG and blood pressure monitoring and water/electrolyte supplements as needed. A profuse and prolonged aquaresis should be anticipated, which, if not matched by oral fluid ingestion, should be replaced with intravenous hypotonic fluids, while closely monitoring electrolytes and fluid balance.

ECG monitoring should begin immediately and continue until ECG parameters are within normal ranges. Dialysis may not be effective in removing tolvaptan because of its high binding affinity for human plasma protein (>99%). Close medical supervision and monitoring should continue until the patient recovers.

PATIENT COUNSELING INFORMATION: As a part of patient counseling, healthcare providers must review the SAMSCA Medication Guide with every patient *[see FDA-Approved Medication Guide (17.3)]*.

Concomitant Medication: Advise patients to inform their physician if they are taking or plan to take any prescription or over-the-counter drugs since there is a potential for interactions.**Strong and Moderate CYP 3A inhibitors and P-gp inhibitors:** Advise patients to inform their physician if they use strong (e.g., ketoconazole, itraconazole, clarithromycin, telithromycin, nelfinavir, saquinavir, indinavir, ritonavir) or moderate CYP 3A inhibitors (e.g., aprepitant, erythromycin, diltiazem, verapamil, fluconazol) or P-gp inhibitors (e.g., cyclosporine) *[see Dosage and Administration (2.3), Contraindications (4.4), Warnings and Precautions (5.5) and Drug Interactions (7.1)]*.

Nursing: Advise patients not to breastfeed an infant if they are taking SAMSCA *[see Use In Specific Populations (8.3)]*.

For more information about SAMSCA, call 1-877-726-7220 or go to www.samsca.com.

Manufactured by Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan

Distributed and marketed by Otsuka America Pharmaceutical, Inc., Rockville, MD 20850

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INDICATION and Important Limitations

- SAMSCA is indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium <125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH)
- Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with SAMSCA. It has not been established that raising serum sodium with SAMSCA provides a symptomatic benefit to patients

IMPORTANT SAFETY INFORMATION

SAMSCA should be initiated and re-initiated in patients only in a hospital where serum sodium can be monitored closely. Too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours) can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death. In susceptible patients, including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable

Contraindications: Urgent need to raise serum sodium acutely, inability of the patient to sense or appropriately respond to thirst, hypovolemic hyponatremia, concomitant use of strong CYP 3A inhibitors, anuric patients, and hypersensitivity (e.g. anaphylactic shock, rash generalized) to tolvaptan or its components

Warnings and Precautions:

- Subjects with SIADH or very low baseline serum sodium concentrations may be at greater risk for too-rapid correction of serum sodium. In patients receiving SAMSCA who develop too rapid a rise in serum sodium or develop neurologic sequelae, discontinue or interrupt treatment with SAMSCA and consider administration of hypotonic fluid. Fluid restriction should generally be avoided during the first 24 hours
- SAMSCA can cause serious and potentially fatal liver injury. Avoid use in patients with underlying liver disease, including cirrhosis, because the ability to recover may be impaired. Limit duration of therapy with SAMSCA to 30 days
- Dehydration and hypovolemia can occur, especially in potentially volume-depleted patients receiving diuretics or those who are fluid restricted. In patients who develop medically significant signs or symptoms of hypovolemia, discontinuation is recommended
- Co-administration with hypertonic saline is not recommended
- Avoid concomitant use with: CYP 3A inhibitors and CYP 3A inducers. The dose of SAMSCA may have to be reduced if co-administered with P-gp inhibitors
- Monitor serum potassium levels in patients with a serum potassium >5 mEq/L and in patients receiving drugs known to increase serum potassium levels

Adverse Reactions - The most common adverse reactions (SAMSCA incidence ≥5% more than placebo, respectively): thirst (16% vs 5%), dry mouth (13% vs 4%), asthenia (9% vs 4%), constipation (7% vs 2%), pollakiuria or polyuria (11% vs 3%) and hyperglycemia (6% vs 1%)

Gastrointestinal Bleeding in Patients with Cirrhosis – In patients with cirrhosis in the hyponatremia trials, GI bleeding was reported in 10% of tolvaptan-treated patients vs 2% for placebo

Please see Brief Summary of FULL PRESCRIBING INFORMATION, including Boxed WARNING, on following page.

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For more information please visit SAMSCA.com

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