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Press Release

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ASN KIDNEY WEEK 2014 • NOVEMBER 11–16 • PHILADELPHIA, PA

ASN KIDNEY WEEK LATE-BREAKING CLINICAL STUDIES HIGHLIGHT ADVANCES IN KIDNEY CARE

Philadelphia, PA (November 15, 2014) — The results of numerous high-impact clinical trials that could affect kidney-related medical care will be presented at ASN Kidney Week 2014 November 11–16 at the Pennsylvania Convention Center in Philadelphia, PA.

Among the studies are the following (presented in numerical order):

SA-PO1092 A Randomized Multicomponent Intervention to Reduce Disparities in Transplant Referral: Interim Results from the RaDIANT Community Study — Rachel E. Patzer, Leighann Sauls, Jennifer C. Gander, M. Ahinee Amamoo, Laura Plantinga, Debra D. Evans, Eric M. Gibney, Laura L. Mulloy, Stephen O. Pastan. Atlanta, GA.

The Southeastern United States, and in particular the state of Georgia, has the lowest rate of kidney transplantation in the nation. The Reducing Disparities In Access to kidNey Transplantation (RaDIANT) Community Study was developed by the academic and community partnership the Southeastern Kidney Transplant Coalition of Georgia, North Carolina, and South Carolina to reduce disparities in access to kidney transplantation among African American End Stage Renal Disease patients. We randomized 134 dialysis facilities in GA that had racial disparity in referral and/or low transplant referral to receive several provider and patient education and engagement interventions (n=67) or no intervention (n=67) over a period of one year (Jan-Dec 2013) in order to improve transplant referrals. Intervention activities included educational webinars for staff, staff- and patient-level educational activities, monthly monitoring of quality improvement activities, and traditional quality improvement oversight of transplant referral overseen by our Southeastern Kidney Transplant Coalition partner End Stage Renal Disease Network 6.

Interim 6-month results among intervention facilities show that the proportion of patients referred for transplant within a facility more than doubled among all of the intervention patients, and more than tripled among African American patients. By 6 months, more than half of the dialysis facilities had eliminated racial disparity in kidney transplant referrals. While the intervention is ongoing through Dec. 2014, preliminary results suggest that the interventions delivered in the RaDIANT Community may increase access to

transplant referral and reduce African American vs. white racial disparity in transplant referral access. Longer-term follow-up is needed to examine how these interventions impact access to waitlisting and transplantation. The integration of a sustainable, long-term community-based intervention to improve access to kidney transplant referrals may have a long-lasting impact on the reduction of disparities in kidney transplantation.

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SA-PO1102 Ferric Citrate Safely Controls Phosphorus, Delivers Iron, and Reduces IV Iron/ESA in ESRD: A 48-Week Clinical Trial — Julia Lewis, Kausik Umanath, Mohammed Sika, Mark Koury, Peale Chuang, Gerald Schulman, Robert M. Niecestro, Tom Greene, Jamie P. Dwyer, The Collaborative Study Group. Nashville, TN.

Patients with ESRD require multiple medications to manage both their bone and mineral metabolic disturbances and their chronic anemia. The PERFECTED study (PhosphatE binding and iRon delivery with Ferric CiTrate in EsrD) demonstrated that ferric citrate was a highly effective phosphate binder in a 4-week placebo controlled period and achieved similar serum phosphorus levels compared to active control in a 52-week active control period requiring fewer doses compared to sevelemar carbonate to achieve this. In addition and importantly in the 52-week active control period, ferric citrate had highly statistically significant and beneficial effects on these subjects chronic anemia including; increased iron stores as evidenced by increased serum ferritin and TSAT; decreased IV iron and ESA usage; and sustained hemoglobin compared to active control. These findings were associated with an excellent safety profile with fewer subjects experiencing any SAE, an infection (ID) associated SAE, a cardiovascular (CV) associated SAE or a gastrointestinal (GI) associated SAE compared to active control. Subsequent analysis also demonstrated significant projected health care cost savings related to reduced hospitalizations and reduced usage of IV iron and ESA. The study reported here at ASN is a 48-week pragmatic trial that enrolled 168 of the 441 subjects that participated in the PERFECTED study in an additional 48-week trial where all subjects received ferric citrate. Over the 48-week trial serum phosphorus was again well controlled with ferric citrate (mean baseline serum phosphorus 5.7 mg/dL, 48-week serum phosphorus 5.2 mg/dL). On ferric citrate, iron stores increased and the study demonstrated plateauing of both the serum ferritin and the TSAT at 48 weeks. This supports the hypothesis that iron absorption from ferric citrate is tightly regulated in the GI tract. IV iron and ESA usage were again decreased over time and hemoglobin levels sustained. In this study 60% of the subjects never required a single dose of IV iron and in the last 12 weeks of this study 85% of subjects were not receiving IV iron. This is in contrast to the DOPPS data which reports 70-80% of dialysis patients are receiving IV iron at any given time. Ferric citrate use extended now over an additional 48 weeks also had a safety profile comparable to that reported during the original 52 week trial as evidenced by a similar occurrence of overall SAE's, and specifically ID, CV and GI associated SAE's. The use of ferric citrate over 100 weeks retains its efficacy and safety profiles with iron stores plateauing and no safety concerns identified.

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SA-PO1104 Phase III Study of ASP1585 (Bixalomer) – Randomized, Double-Blind, Placebo-Controlled Study in Chronic Kidney Disease Patients with Hyperphosphatemia Not on Dialysis — Tadao Akizawa, Hideki Origasa, Chisato Kameoka, Junko Tsukada, Kentarou Kuroishi, Yusuke Yamaguchi. Tokoyo, Japan.

ASP1585 (Bixalomer) is a non-absorbable polymer that decreases serum phosphorus level by binding phosphate in the gastrointestinal tract. This is a phase III trial to demonstrate efficacy by showing superiority of ASP1585 to placebo, and evaluate safety profile in Japanese CKD patients with hyperphosphatemia not on dialysis. The primary endpoint (change from baseline in serum phosphorus level at the end of treatment) in ASP1585 showed a statistically significant difference compared to placebo. Incidences of adverse events were comparable between ASP1585 and placebo. In conclusions, ASP1585 was effective in decreasing serum phosphorus level, while showing a well-tolerated safety profile compared to placebo. These findings indicated the clinical benefits of ASP1585 as a treatment for hyperphosphatemia in CKD patients not on dialysis.

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SA-PO1105 2MD, a New Treatment for Secondary Hyperparathyroidism — Hector F. Deluca. Madison, WI.

A novel analog of 1α,25-dihydroxyvitamin D_3, 2-methylene-(20S)-19-nor-1α,25-dihydroxyvitamin D_3 (2MD or DP001) has been developed that localizes selectively in the parathyroid cells. It markedly suppresses parathyroid hormone synthesis/secretion with little or no change in serum calcium and calcium x phosphorus product. A Phase 2B, 12-week, pivotal double-blinded, placebo-controlled trial in 62 stage 5 renal failure patients has been completed. Both primary and secondary efficacy endpoints were achieved. No patient reached the serum calcium safety threshold of two consecutive serum calcium values of >11.0 mg%. In patients previously on an active vitamin D (AVD) compound or an AVD plus a calcimimetic, 2MD, at 220-770 ng oral 3X/week at dialysis, successfully suppressed PTH by 46% in more than 80% of the patients. 2MD is safe and efficacious at a wide dosage range and is further able to manage patients previously on an AVD plus a calcimimetic.

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SA-PO1106 Iron Isomaltoside 1000 (Monofer®) Compared to Oral Iron Sulphate in Patients with Non-Dialysis Dependent Chronic Kidney Disease (NDD-CKD) — Philip A. Kalra, Sunil Bhandari, Lars L. Thomsen. Salford, United Kingdom.

Iron deficiency anemia (low haemoglobin levels) is common in patients with chronic kidney disease and is often treated with iron therapy. This study compared the effect and safety of a newer iron preparation, iron isomaltoside 1000, which is injected into the

patient, with traditional tablets of iron sulphate in non-dialysis patients with chronic kidney disease and anaemia who were not receiving eythropoeitins.

Iron isomaltoside 1000 increased hemoglobin significantly better than iron given as tablets. The effect was observed 3 weeks after the treatment was initiated and it was sustained until the end of the trial at week 8 with an increase in effect week by week. The number of side effects observed with the two treatments was similar; however, more patients treated with iron tablets withdrew from the study due to side effects (4.2% versus 1.3%).

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SA-PO1107 In-Hospital, Electronic Alerts for Acute Kidney Injury: A Randomized, Controlled Trial — Francis Perry Wilson, Michael G. Shashaty, Peter P. Reese, Yevgeniy Gitelman, Yuliya Borovskiy, Harold I. Feldman, Susan Ellenberg, Barry D. Fuchs. New Haven, CT.

Acute Kidney Injury (AKI), a leading cause of morbidity and mortality in hospitalized patients, may go unrecognized by care providers. In this study, Dr. F. Perry Wilson of Yale University School of Medicine and Colleagues sought to evaluate the effect of an electronic AKI alert system. Over one year, 2400 patients at the Hospital of the University of Pennsylvania were randomized to receive AKI alerts or usual care. For those in the AKI alert arm, the primary in-hospital provider and unit pharmacist would receive a text page informing of the presence of AKI. The primary outcome was a composite of change in creatinine, dialysis, and death within 7 days of randomization.

Alerts were well received by providers, with over 70% stating they would like to continue receiving alerts after the study ended. However, there was no improvement in the primary outcome between the two groups (p=0.12). The overall rates of dialysis and death were, in fact, slightly higher in the alert arm of the study (7.2% vs. 5.9%, p=0.18 for dialysis and 5.9% versus 5.1%, p=0.40 for death) though these did not achieve statistical significance. Process measures such as the administration of contrast media were also not significantly different between the groups. The authors concluded that, if an alert system is to be implemented, it should be carefully targeted to those most susceptible to missed diagnosis, and not broadly applied to all patients with AKI.

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SA-PO1108 A Randomized Trial of Home Video Monitoring by an Interprofessional Care Team on Outcomes in Patients with Chronic Kidney Disease — Areef Ishani, Juleen Christopher, Deirdre A. Palmer, Sara Otterness, Barbara Clothier, Sean Nugent, David Nelson, Mark E. Rosenberg. Minneapolis, MN.

Managing patients at home using video technology (telehealth) and the use of an interprofessional case management team are newer strategies of care that have effectively been used to care for patients with chronic diseases. Chronic Kidney Disease (CKD) is common and associated with a significant number of other illnesses and poor

patient outcomes. It is unknown if using telehealth and an interprofessional team improves patient outcomes in patients with CKD. We conducted a randomized controlled trial in which 450 patients were randomized to receive an intervention consisting of care by an interprofessional team (nephrologist, nurse practitioner, nurses, clinical pharmacy specialist, psychologist, social worker, dietician) using a telehealth device (touch screen computer, webcam, blood pressure cuff, scale, and glucometer), and another 150 patients were randomized to usual care. The primary patient outcome for the study was a combination of death, hospitalization, emergency department visits, or admission to a nursing home.

At the beginning of the study our patients had the following characteristics: average age, 75.1 ± 8.1 years; male, 98.5%; white, 97.3%; an average level of kidney function of about 40% compared to normal. One year after randomization at the time the study was finished, 70 (46.7%) patients in the usual care group vs. 208 (46.2%) in the intervention group experienced the primary combination outcome (P = 0.90, hazard ratio 0.98, 95% confidence interval 0.75 – 1.29). There was no difference between groups for any individual outcome including: all-cause mortality (1.46, 0.42-5.11), hospitalization (1.15, 0.80-1.63), emergency department visits (0.92, 0.68-1.24), or nursing home admission (3.07, 0.71-13.24).

Telehealth by an interprofessional team did not improve health outcomes in patients with moderate to severe CKD compared with usual care. Strategies for improving the care of this population are needed. Future disease management strategies should be rigorously evaluated before widespread implementation.

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SA-PO1109 Stent Treatment in Atherosclerotic Renal Artery Stenosis: Kidney Function and Clinical Events — Katherine R. Tuttle, Lance D. Dworkin, Barbara A. Greco, William L. Henrich, Michael Steffes, Kenneth A. Jamerson, Joseph I. Shapiro, Karol M Pencina, Joseph Massaro, Donald Cutlip, Sheldon W. Tobe, Timothy P. Murphy, Christopher J. Cooper, Ralph B. D'Agostino.
Spokane, WA.

The effect of renal artery revascularization by stenting on chronic kidney disease (CKD) in people with atherosclerotic renal artery stenosis (ARAS) has remained uncertain despite two recent clinical trials (STAR and ASTRAL, 2009).These, and other, prior clinical trials did not demonstrate lasting benefit of stenting on kidney function or clinical event outcomes, but may have been under-powered or lacking in ascertainment. In the Cardiovascular Outcomes in Renal Artery Stenosis (CORAL) Trial, people with ARAS were randomized to renin-angiotensin system (RAS) inhibition-based medical therapy plus stenting or medical therapy alone. The trial had a large, international sample and long-term follow-up that provide unique opportunity to assess the longitudinal effect of stenting on kidney function and predictors of attendant clinical events.

Key findings:

- The eGFR did not differ between treatment groups at baseline or over time.
- In the combined groups, eGFR was 59+/-24 ml/min/1.73m^2 (mean+/-SD, creatinine-cystatin-C CKD-EPI) at baseline and 53+/-22 ml/min/1.73m^2 after 4 years.
- The CKD event outcome (death, end-stage renal disease, >30% eGFR loss occurred in 19 % (175/931).
- The CVD event outcome (death, stroke, myocardial infarction, heart failure) occurred in 22 % (207/931).

Stent treatment added to medical therapy did not improve eGFR. At baseline, eGFR was mildly decreased and declined slightly over 4 years. Predictors of longitudinal eGFR were established CKD risk factors in multiple variable models. Neither stent treatment nor more severe ARAS (bilateral) predicted eGFR. Stent also treatment did not did not reduce risk of CKD or CVD events. Predictors of these events were traditional risk factors, markers of CKD severity, and bilateral ARAS (CVD only). In conclusion, stent treatment did not improve kidney function or reduce risk of CKD or CVD events in CORAL participants with ARAS receiving RAS inhibition-based medical therapy.

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ASN Kidney Week 2014
Saturday, November 15, 2014
Late-Breaking Posters
Exhibit Halls A–C

Additional Posters Include:

SA-PO1091 Levofloxacin for BK Virus Prophylaxis in Kidney Transplantation — John S. Gill, Atul Humar, Dean Fergusson, Olwyn Johnston, Andrew A. House, Jo seph Kim, Tim Ramsay, Michaël Chassé, Xiaoli L Pang, Jeffrey S. Zaltzman, Sandra M. Cockfield, Marcelo Cantarovich, Martin Karpinski, Louise Lebel, Greg A. Knoll. Vancouver, BC, Canada.

SA-PO1093 Envarsus XR (Once-Daily MeltDose Tacrolimus Tablets) Shows Continued Dose Reduction and Similar Efficacy and Safety vs. Prograf (Twice-Daily Tacrolimus Capsules) at Two-Years: Results of a Phase 3, Double-Blind, Randomized Study in De Novo Kidney Transplant Patients — Lionel Rostaing, Suphamai Bunnapradist. Toulouse Cedex, France.

SA-PO1094 Urgent-Start Peritoneal Dialysis versus Urgent-Start Hemodialysis: A Multicenter Clinical Trial — Arshia Ghaffari, Steven M. Brunelli, Michelle Cassin, Martin J. Schreiber. Los Angeles, CA.

SA-PO1095 Standard versus Accelerated Initiation of Renal Replacement Therapy in Acute Kidney Injury — Ron Wald, Neill Adhikari, Karen L. Pope, Orla M. Smith, Matthew A. Weir, Sean M. Bagshaw. Toronto, ON, Canada.

SA-PO1096 The Utility of Photoplethysmographic Measures of Cardiovascular Stress to Detect Intradialytic Hypotension — Dana Miskulin, Klemens B. Meyer, Mary kay Deck, Anne M. Brumfield, Rajat Deo, John E. Moran. Sommerville, MA.

SA-PO1097 The Beta-Blocker to LOwer CArdiovascular Dialysis Events (BLOCADE) Feasibility Study: A Randomized Controlled Trial of Carvedilol versus Placebo in Patients Receiving Dialysis — Matthew Allan Roberts. Blackburn, VIC, Australia.

SA-PO1098 Migalastat and Enzyme Replacement Therapy Have Comparable Effects on Renal Function in Fabry Disease: Phase 3 Study Results — Kathleen M. Nicholls, Daniel G.
Bichet, Roberto Giugliani, Derralynn A. Hughes, Raphael Schiffmann, William Wilcox, Nina Skuban, Jasmine L. Rutecki, Julie Yu, Jeff Castelli, John R. Kirk, Elfrida R. Benjamin, Jay Barth. Parkville, Australia.

SA-PO1099 Effect of Patiromer on Hyperkalemia in Patients with Diabetic Nephropathy: Results of a 1-Year Randomized Trial — George L. Bakris, Bertram Pitt, Martha Mayo, Dahlia Garza, Yuri Stasiv, Lance Berman, David A. Bushinsky. Chicago, IL.

SA-PO1100 ZS-9 Effectively Reduces Potassium Levels in Hyperkalemic Diabetic Patients Who Have Both Renal Impairment and a History of Heart Failure — David K. Packham, Simon D. Roger, Mohamed A. El-Shahawy, Wajeh Y. Qunibi, Henrik S. Rasmussen, Bhupinder Singh, Alex Yang, Philip T. Lavin, Adrian Covic. Eltham Melb, VIC, Australia.

SA-PO1101 Empagliflozin Reduces Blood Pressure and Markers of Arterial Stiffness and Vascular Resistance in Type 2 Diabetes — Robert Chilton, Ilkka T. Tikkanen, Christopher Paul Cannon, Susanne Crowe, Thomas Hach, Hans-Juergen Woerle, Uli Christian Broedl, Odd Erik Johansen. San Antonio, TX.

SA-PO1103 Safety and Efficacy of Modified-Release Calcifediol for Secondary Hyperparathyroidism in Patients with Stage 3 or 4 CKD and Vitamin D Insufficiency — Stuart M. Sprague, Shaukat Ali, Roberto Mangoo-Karim, Paul W. Crawford, Pablo E. Pergola, Laurel Sindelar, Stephen A Strugnell, Joel Z. Melnick, Jay A. White, Martin P. Petkovich, Charles W. Bishop. Chicago, IL.

Disclosure information is available at

http://www.asn-online.org/education/kidneyweek/2014/program-faculty.aspx.

ASN Kidney Week 2014, the largest nephrology meeting of its kind, will provide a forum for more than 13,000 professionals to discuss the latest findings in renal research and engage in educational sessions related to advances in the care of patients with kidney and related disorders. Kidney Week 2014 will take place November 11–16, 2014 in Philadelphia, PA.

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Founded in 1966, and with more than 15,000 members, the American Society of Nephrology (ASN) leads the fight against kidney disease by educating health professionals, sharing new knowledge, advancing research, and advocating the highest quality care for patients.

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