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OCTOBER 26 AT 10:30 AM PT (1:30 PM ET)**

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HIGH-IMPACT CLINICAL TRIALS YIELD RESULTS THAT COULD IMPROVE KIDNEY CARE

San Diego, CA (October 25, 2018) — The results of numerous high-impact clinical trials that could affect kidney-related medical care will be presented at ASN Kidney Week 2018 October 23–October 28 at the San Diego Convention Center.

- Because type 2 diabetes is a common cause of kidney failure, the effects of glucose-lowering therapies on kidney outcomes are of great interest. The double-blind CARMELINA trial randomized people with type 2 diabetes and CKD to receive linagliptin (a DPP inhibitor) or placebo. Linagliptin slowed progression of albuminuria, without affecting other kidney outcomes. Linagliptin also demonstrated cardiovascular safety including in patients with advanced CKD, where clinical evidence has been particularly scarce. “The CARMELINA trial specifically demonstrated that linagliptin is safe from a CV perspective in people with kidney disease as well as overall. It found that linagliptin facilitates the safe improvement of glycemic control in people with kidney disease, who currently have limited options available to them,” said Vlado Perkovic, MBBS, PhD, FRACP, FASN, lead author of the study.
Effect of Linagliptin on Kidney and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Kidney Disease: CARMELINA®.
- Intravenous (IV) iron is widely used in the management of anemia in hemodialysis patients, but very little scientific evidence guides its appropriate use. The Proactive IV irOn Therapy in haemodiALysis patients (PIVOTAL) trial was designed to compare the effects of 2 distinct IV iron dosing regimens on clinical outcomes, including mortality and cardiovascular events, as well as infection risk among hemodialysis patients. In the multicenter, open-label, blinded endpoint, controlled trial, 2141 hemodialysis patients receiving erythropoiesis-stimulating agents were randomly assigned to a proactive, high-dose IV iron regimen or a reactive, low-dose IV iron regimen. “Patients receiving haemodialysis usually require Erythropoiesis Stimulating Agents—ESAs—to treat their anaemia. High doses of ESAs are potentially harmful, so we try to use low doses and enhance the patient’s response by adding IV iron. Over recent years we have tended to give more iron and less ESAs, but the optimal balance between these therapies is not known,” explained co-author David Wheeler, MBChB, MD, FRCP. “The PIVOTAL trial investigated whether giving higher doses of IV iron could be harmful, as suggested by previous observational studies. As compared to a lower dose, we found no evidence of harm when using a higher dose of IV iron and were able to reduce ESA doses and blood

transfusions. A high dose iron, low dose ESA strategy could provide a safer approach to treating anaemia in haemodialysis patients and needs to be further evaluated in larger studies.”

High-Dose versus Low-Dose Intravenous Iron Therapy in Hemodialysis: The PIVOTAL Trial

- High blood glucose levels exacerbate the progression of CKD, but most glucose-lowering therapies seldom address morbidities associated with CKD. Sodium-glucose cotransporter-2 (SGLT2) inhibitors are relatively new diabetes drugs that are associated with benefits beyond glucose control, including weight loss, decreased blood pressure, and improved lipid profiles—but their effectiveness may be diminished with impaired kidney function. In a phase 3 randomized trial, the utility of bexagliflozin (a highly specific SGLT2 inhibitor) was studied in patients with stage 3 CKD and poorly controlled type 2 diabetes. In the trial, 312 patients were randomly assigned to receive bexagliflozin or placebo for 24 weeks. Participants who received bexagliflozin had a significant reduction of hemoglobin A1c (a measure of blood glucose), weight loss, lower blood pressure, and less protein in the urine. “Roughly one third of diabetics suffer from stage 3 CKD. This study suggests that bexagliflozin could be of benefit to this group,” said lead author Andrew Allegretti, MD, MSc. *Safety and Effectiveness of Bexagliflozin in Type 2 Diabetes Mellitus and Stage 3a/3b Chronic Kidney Disease, a Phase III Randomized Clinical Trial*
- Safely reducing red blood cell transfusions avoids transfusion-related adverse effects, conserves the blood supply, and reduces healthcare costs. In an international clinical trial of over 4500 patients undergoing cardiac surgery with cardiopulmonary bypass, patients were assigned to a restrictive red blood cell transfusion threshold (transfuse if hemoglobin level was <7.5 g/dL, intraoperatively and postoperatively until day 28 or hospital discharge) or a liberal threshold (transfuse if hemoglobin level was <9.5 g/dL in the operating room or intensive care unit, or <8.5 g/dL on the non-intensive care ward). Acute kidney injury occurred in 27.7% of patients in the restrictive-threshold group and in 27.9% of patients in the liberal-threshold group. “We learned a restrictive approach to red blood cell transfusion is as safe as a liberal approach with respect to the risk of injuring the kidneys,” said Amit Garg, MD, PhD, lead author of the study. *Effect of a Restrictive Versus Liberal Approach to Red Blood Cell Transfusion on Acute Kidney Injury in Patients Undergoing Cardiac Surgery*
- There are higher healthcare costs and poorer outcomes when patients initiate dialysis earlier at a higher level of kidney function compared with when they initiate dialysis later. A clinical trial evaluated the impact on chronic kidney disease (CKD) clinics of an educational intervention aimed at delaying the start of dialysis. In the trial, 27 clinics received the educational tools and 28 did not. “At the end of study, there was no difference in early dialysis starts between both sets of clinics,” said lead author Navdeep Tangri, MD, PhD, FRCPC. “This is because an improvement in

dialysis timing had already begun in the entire country before our trial started. We are now working on analyses to examine whether our intervention affected pre-dialysis outcomes.”

Interventions to Reduce Early Dialysis Initiation in Canada: A Cluster Randomized Trial

- Depression is common in patients undergoing hemodialysis but limited data exist on increasing treatment acceptance or efficacy of various anti-depressant therapies. A multi-center randomized trial compared the efficacy of cognitive behavioral therapy (a form of psychotherapy) vs. sertraline (an anti-depressant drug) for treating depression in patients undergoing hemodialysis. “Depressive symptoms improved with both treatments but the improvement was greater with sertraline; however, adverse events were also more frequent with sertraline,” said Raj Mehrotra, MD, lead author of the study. “Future studies should test treatments that are more effective in improving depressive symptoms without the associated adverse events.”
Comparative Efficacy of Therapies for Depression for Patients Undergoing Hemodialysis
- Joseph V. Bonventre, MD, PhD will announce that ASN's Kidney Health Initiative is issuing its Technology Roadmap for Innovative Approaches to Renal Replacement Therapy (RRT). The patient-centered, multidisciplinary roadmap encourages much needed innovative alternatives to kidney dialysis. **The embargo for this announcement lifts on Thursday, October 25 at 9:45 am PT.**

ASN Kidney Week 2018, the largest nephrology meeting of its kind, will provide a forum for more than 13,000 professionals to discuss the latest findings in kidney health research and engage in educational sessions related to advances in the care of patients with kidney and related disorders. Kidney Week 2018 will take place October 23 – October 28 at the San Diego Convention Center.

Since 1966, ASN has been leading the fight to prevent, treat, and cure kidney diseases throughout the world by educating health professionals and scientists, advancing research and innovation, communicating new knowledge, and advocating for the highest quality care for patients. ASN has more than 20,000 members representing 131 countries. For more information, please visit www.asn-online.org.

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