PRESS RELEASE

ASN Contact:
Christine Feheley (202) 640-4638 | cfeheley@asn-online.org

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

San Diego (November 5, 2021) — The results of numerous high-impact clinical trials that could affect kidney-related medical care will be presented online at ASN Kidney Week 2021 November 4–November 7.

- Primary hyperoxaluria type 1 (PH1) is a rare genetic disorder characterized by overproduction of oxalate by the liver, leading to progressive kidney disease. In the ILLUMINATE-C phase 3 study, patients with PH1 and chronic kidney disease (including patients on hemodialysis) who were treated with lumasiran ((an RNAi therapeutic indicated for the treatment of PH1 to lower urinary oxalate levels in pediatric and adult patients) experienced substantial reductions in plasma oxalate. "We know that high plasma oxalate levels are associated with severe and potentially life-threatening complications, including deposition of oxalate in the heart, bones, skin and eyes of these patients—a condition known as systemic oxalosis—resulting in multiorgan dysfunction," said lead author Mini Michael, MD, Pediatric Nephrologist, Baylor College of Medicine/Texas Children's Hospital. "Thus, a drop in oxalate levels of the magnitude seen in this study is promising and we hope will translate into improved long-term clinical outcomes, including oxalosis, which is something that we plan to further evaluate in the ILLUMINATE-C extension period." *ILLUMINATE-C, a Single-Arm, Phase 3 Study of Lumasiran in Patients with Primary Hyperoxaluria Type 1 and CKD Stages 3b-5, Including Those on Hemodialysis*

- IgA nephropathy is a common cause of kidney failure, especially among young people, but no specific treatments have been shown to prevent important kidney outcomes to date. The Therapeutic Evaluation of STeroids in IgA Nephropathy Global (TESTING) study assessed the effects of oral methylprednisolone compared with placebo on major kidney outcomes and safety in patients with IgA nephropathy. In total, 503 participants were randomized to methylprednisolone (257) or placebo (246), including 262 to a full dose (0.6-0.8 mg/kg/day, maximum 48 mg/day, for 2 months then weaning by 8 mg/day/month) or placebo and 241 to a reduced dose (0.4 mg/kg/day, maximum 32 mg/day, weaning by 4 mg/day/month) or placebo. Over an average follow-up of 4.2 years, methylprednisolone reduced the risk of the primary outcome (composite of 40% eGFR decline or kidney failure) by 47% and kidney failure by 41%. The reduction in risk was seen with both doses. Serious

adverse events were more frequent with methylprednisolone vs. placebo (28 vs. 7 patients), particularly with the full dose (22 vs. 4) compared with the reduced dose (6 vs. 3). “The TESTING trial showed that two different doses of a cheap type of oral steroid taken for 6 to 9 months reduced the risk of major kidney events and kidney failure. The risk of adverse events, especially infections, was increased mainly with high-dose treatment, suggesting that reduced-dose therapy best balances risks and benefits,” said co–senior author Vlado Perkovic, MBBS, PhD, of the University of New South Wales, in Australia.
The TESTING Study: Steroids vs. Placebo in High Risk IgA Nephropathy

- In EMPEROR-Preserved, the sodium-glucose co-transporter 2 inhibitor empagliflozin reduced cardiovascular deaths and heart failure hospitalizations and slowed kidney function decline in patients with heart failure and a preserved ejection fraction (HFpEF), with or without diabetes. A new analysis of the trial’s data showed that these benefits were experienced in patients regardless of the presence or absence of chronic kidney disease and across a broad spectrum of baseline kidney function. The analysis included 5,988 patients who were randomized, of whom 3,198 (53%) had prevalent chronic kidney disease. “As part of the active, and so far disappointing quest for a therapy to help patients with HFpEF, the EMPEROR-Preserved trial is the first trial showing unequivocal cardiac and renal benefits in such patients. This trial reproduces the same benefits also observed in patients with heart failure and reduced ejection fraction,” said lead author Faiez Zannad, MD, PhD, of Université de Lorraine, Inserm INI-CRCT, in France. “Therefore, empagliflozin is the first drug ever showing a consistent improvement of cardiovascular outcomes and a slowing of kidney function decline across the full spectrum of kidney function, including patients with chronic kidney disease, across the full spectrum of cardiac ejection fraction and in patients with and without diabetes.”
  EMPEROR-Preserved: Empagliflozin and Outcomes in Heart Failure with a Preserved Ejection Fraction and CKD

- Nephrotic syndrome is one of the most common kidney diseases in children. Previous studies suggest that 8–12 weeks of prednisone is an effective and safe initial treatment. There is preliminary evidence that young children (<6 years old) might experience fewer relapses if the duration of initial therapy is prolonged to 16–24 weeks. In an open label multicenter study, investigators randomly assigned 172 young children <4 years of age to either receive 12 weeks or 24 weeks of prednisone as initial therapy. Proportions of patients with sustained remission and frequent relapses at 1- and 2-years, time to relapse or frequent relapses, and relapse rates were all similar in the 2 groups. “Our findings suggest that prolonging initial therapy beyond 12 weeks does not significantly impact the subsequent frequency of relapses,” said lead author Aditi Sinha, MD, MBBS, PhD, of the All India Institute of

Medical Sciences, in New Delhi. “Young children with the first episode of nephrotic syndrome should receive similar treatment as older children.”
Randomized Controlled Trial Comparing 3- vs. 6-Months Initial Prednisone Therapy in Young (<4-Year-Old) Children with Nephrotic Syndrome

- In patients with chronic kidney disease (CKD), anemia is often underdiagnosed and undertreated, even though it’s a significant complication of CKD. The ASCEND program, which consists of more than 8,000 patients with CKD, includes two pivotal phase 3 studies investigating the efficacy and cardiovascular safety of daprodustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, as a novel alternative to injectable erythropoiesis-stimulating agents (ESAs), the current standard of care. These studies independently met their primary safety and efficacy endpoints, showing daprodustat improved or maintained hemoglobin with no increased cardiovascular risk compared with ESAs across both dialysis and non-dialysis patients. “Evidence found that daprodustat is an oral option as effective and safe as an ESA and is well tolerated, which underscores that using an oral agent, such as daprodustat, could help improve accessibility and compliance for patients with anemia of CKD who ordinarily can’t access treatment because in many patients, ESA needs to be administered by a health care provider,” said lead author and chair of the steering committee for the ASCEND program Ajay Singh, MBBS, FRCP (UK), MBA, a nephrologist at Brigham and Women’s Hospital and Harvard Medical School. “In addition to stimulating natural production of erythropoietin, daprodustat causes changes in markers of iron metabolism in the body, which may heed a benefit, and it works well in patients who have poor response to ESA.”
ASCEND Program: Efficacy and Safety from ASCEND-D and -ND and Overall MACE Finding

- Chlorthalidone was approved by the U.S. Food and Drug Administration for the treatment of hypertension in 1960, but it is currently only prescribed for people without advanced kidney disease. In the chlorthalidone in chronic kidney disease (CLICK) study, 160 patients with hypertension and stage 4 chronic kidney disease were randomized to placebo or chlorthalidone. This low-cost medication lowered blood pressure in patients within 4 weeks, and this lowering was sustained over a 12-week treatment period. The adjusted change from baseline in 24-hour systolic blood pressure was -0.5 mm Hg in the placebo group and -11.0 mm Hg in the chlorthalidone group. Furthermore, the drug lowered albuminuria (a marker of kidney dysfunction) by 50% over 12 weeks, suggesting that it may have kidney-protective effects. “Besides the adverse effects we commonly see with the use of this drug in people without kidney disease, we saw an increased risk of reversible changes in kidney function, particularly when people were also receiving medications called loop diuretics,” said lead author Rajiv Agarwal, MD, of the Indiana University School of

Medicine and the Roudebush VA, Indianapolis. “Thus, careful monitoring is required when using this medication.”
Chlorthalidone for Hypertension in Advanced CKD (CLICK): A Randomized Double-Blind Trial

- The Ellipsys Pivotal Trial demonstrated the early safety and efficacy of a minimally invasive procedure to create an arteriovenous fistula in the arms of patients needing hemodialysis. In a recent analysis of long-term data, investigators found that this procedure provided durable access for hemodialysis through 5 years with a high rate of fistula use, and low rates of secondary procedures and complications. “The data demonstrate safety, effectiveness, and durability of the Ellipsys fistula as an alternative to surgery for patients needing dialysis,” said lead author Jeffrey Hull, MD, of the Richmond Vascular Center. “In ongoing studies, the costs and clinical benefits of the Ellipsys fistula are being further evaluated.”
  Long-Term Results of the Ellipsys Percutaneous Fistula for Hemodialysis

- In the phase 3 ADVOCATE trial, patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (a group of autoimmune diseases characterized by inflammation and damage to small blood vessels) were randomized to receive avacopan, an oral inhibitor of the C5a complement receptor, or prednisone taper on a background of either cyclophosphamide (followed by azathioprine) or rituximab. Patients in the avacopan group experienced greater recovery of kidney function compared with patients in the prednisone group, especially patients with advanced kidney dysfunction.
  Effect of Avacopan, a Selective C5a Receptor Inhibitor, on Kidney Function in Patients with ANCA-Associated Vasculitis

ASN Kidney Week 2021, the largest nephrology meeting of its kind, will provide a forum for nephrologists and other kidney health professionals to discuss the latest findings in research and engage in educational sessions related to advances in the care of patients with kidney diseases and related disorders.

Since 1966, ASN has been creating a world without kidney diseases by educating and informing, driving breakthroughs and innovation, and advocating for policies that create transformative changes in kidney medicine throughout the world. ASN has more than 21,000 members representing 131 countries. For more information, visit www.asn-online.org.

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