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New clinical trials reveal insights on treating patients with kidney disease

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Recently completed clinical trials highlight the potential of new therapies for individuals with kidney disease. Below are the findings of two of these studies, which are being presented at ASN Kidney Week 2013 November 5-10 at the Georgia World Congress Center in Atlanta, GA.

Kidney disease can cause abnormally high levels of potassium to accumulate in the blood, a condition called hyperkalemia. This is a serious condition for which physicians lack any safe, reliable, and efficacious treatment options. A phase 2 trial conducted by Stephen Ash, MD (Indiana University Health Arnett, HemoCleanse, Inc. and Ash Access Technology, Inc.) and his colleagues tested the clinical potential of ZS-9, which is an inorganic cation-exchanger that has a crystalline pore and lattice structure to preferentially entrap monovalent cations—specifically, excess potassium ions (K+) over divalent cations such as calcium (Ca2+) and magnesim (Mg2+)—in the gastrointestinal tract. A total of 90 patients with moderate chronic kidney disease and hyperkalemia were randomized into four different groups to receive either placebo or one of three doses of ZS-9 (0.3 g, 3 g, and 10 g). Patients received placebo or ZS-9 orally three times daily.

- ZS-9 was well tolerated, and no serious side effects were reported.
- ZS-9 demonstrated significant dose-dependent reductions in blood K+.
- Within the first 48 hours after treatment initiation, 63% of patients in the 10 g group had ≥1.0 mEq/L reduction in blood K+

compared with only 17% of the placebo cohort.
- With the ZS-9 10 g dose, average blood K+ reduction was rapid and substantial: there was a significant decrease one hour after the initial dose compared with placebo; levels were 0.92 mEq/L lower than baseline after 38 hours of treatment; and levels remained significantly lower than placebo for an additional 3.5 days after the last dose.

"Based on these results, the ongoing clinical program for ZS-9 is designed to explore treatment of acute, subacute, and chronic hyperkalemia. ZS Pharma recently completed the last patient visit in its pivotal phase 3 trial in 750 patients and expects top-line results in the fourth quarter of 2013," said Dr. Ash.

Another team led by Brad Rovin, MD, FASN (Ohio State University Medical Center) assessed the potential of abatacept—a drug that attaches to the surface of inflammatory cells and blocks communication between them—plus standard therapy with the immunosuppressant cyclophosphamide for the treatment of lupus nephritis. This condition is characterized by kidney inflammation caused by the autoimmune disease lupus. The phase 2 trial, called ACCESS, randomized 134 patients with Class III or IV lupus nephritis to placebo or abatacept at weeks 0, 2, 4 and then monthly. All patients received cyclophosphamide.

- At week 24, a total of 33% of patients in the abatacept group and 31% of patients in the control group experienced a complete renal response, which includes stabilization or improvement of kidney function.
- Complete renal response plus partial renal response was 59% in both arms.
- There were no statistically significant differences between groups in the frequency of serious or infectious adverse events, or withdrawals.

- Among complete responders, 50% and 62% of abatacept and control patients respectively, still met complete renal response criteria at week 52, a nonsignificant difference.

"Abatacept plus cyclophosphamide did not improve complete renal response over cyclophosphamide alone," the investigators concluded.

Study: ZS-9, a Novel First-in-Class Hyperkalemia Therapy: Results from a Multicenter, Double Blind, Placebo Controlled, Multiple Dose Study to Evaluate the Effects of ZS 9 in Patients with Chronic Kidney Disease and Hyperkalemia (Abstract 343)

Disclosures: Stephen R. Ash is a consultant for Merit Medical, HemoCleanse, Inc., Fresenius Medical Corporation, and Ash Access Technology, Inc.; has an ownership interest in HemoCleanse, Inc. and Ash Access Technology, Inc. HemoCleanse owns minority share interest in ZS Pharma (a company currently testing an orally ingested drug for removal of potassium), which was originally spun off to its shareholders and the company management; receives research funding from Renal Solutions, Inc. a division of Fresenius Medical Corporation, contracts for device research at HemoCleanse; and honoraria from RMS/DaVita for physician training in peritoneal dialysis catheter placement. Bhupinder Singh is a consultant for Reata, Abbott, Amgen; receives research funding from Amgen, Abbott, Questcor, Otsuka, Kai, Reata, La Jolla, Concert, Hospira, Ardelyx, Keryx; and honoraria from Questcor, Amgen, Reata, Abbott, Medgenics. Philip T. Lavin is a consultant for Boston Biostatistics Research Fdn, and has an ownership interest in ZS Pharma. Fiona Stavros is a consultant for Androscience Corp. and has an ownership interest in ZS Pharma, Inc. Henrik S. Rasmussen is a consultant for Alba Therapeutics, Vaxin; and has an ownership interest in ZS Pharma, Vaxin, Geno, Symphogen.

More information: Study: Treatment of Lupus Nephritis with

Abatacept Plus Low-Dose Pulse Cyclophosphamide: The Results of the ACCESS Trial (Abstract 5807)

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