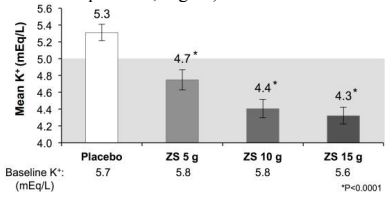
157

SODIUM ZIRCONIUM CYCLOSILICATE (ZS-9) FOR HYPERKALEMIA IN STAGE 4/5 CKD SUBGROUP OF THE PHASE 3 HARMONIZE STUDY. Edgar Lerma[1], Mikhail Kosiborod[1], Henrik S. Rasmussen[2], Philip T. Lavin[3], Alex Yang[2], Wajeh Qunibi[1]; [1]HARMONIZE Study Group; [2]ZS Pharma, Coppell, TX; [3]Boston Biostatistics Research Foundation, Framingham, MA, USA

Hyperkalemia (HK; serum K^+ ≥5.1 mEq/L) is a common and potentially life-threatening electrolyte disorder. Although RAAS inhibitors improve outcomes in pts with CKD, HF and diabetes, and are recommended by practice guidelines, their use is limited by risk for HK. ZS-9 is a nonabsorbed cation exchanger that selectively binds K^+ in the GI tract. The international, multicenter, randomized, double-blind HARMONIZE study demonstrated that ZS-9 rapidly achieved and maintained normal K^+ and was well tolerated. Here we present a subgroup analysis in 84 pts with stage 4 or 5 CKD (eGFR <30mL/min).

Pts with HK received 10g ZS-9 TID for 48h in the acute open-label phase. Those who achieved normokalemia (NK; K^+ 3.5-5.0) were then randomized to QD ZS-9 (5, 10, or 15g) or placebo (PBO) for 28 days.

ZS-9 10g TID significantly reduced serum K^+ (-1.21 mEq/L; P<0.05) at 48h, with 79% of patients achieving normal K^+ by 24 hrs, and 96% by 48 hrs. Serum K^+ was lower with all 3 ZS-9 doses vs. placebo during days 8-29 of the randomized phase (4.7, 4.4 and 4.3 mEq/L for 5, 10 and 15g of ZS-9 respectively; 5.3 mEq/L for placebo, P<0.0001 for all comparisons; Figure).



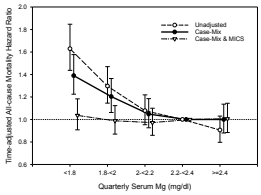
ZS-9 rapidly achieved and maintained normal K^+ for 28 days in HK pts with stage 4 or 5 CKD. These data suggest that ZS-9 is an effective option for treatment of HK, and may optimize the use of the renoprotective RAAS inhibitors in this high risk population.

158

HYPOMAGNESEMIA AND RISK OF ALL-CAUSE MORTALITY IN USA MAINTENANCE HEMODIALYSIS PATIENTS. Lin Li[1]; Elani Streja[1]; Connie M Rhee[1]; Melissa Soohoo[1]; Csaba P Kovesdy[2]; Steven M. Brunelli[3]; Rajnish Mehrotra[4]; Kamyar Kalantar-Zadeh[1]. [1]*UC Irvine, Orange, CA;* [2]*Univ. of Tennessee Health Sciences Center, Memphis, TN;* [3]*Davita Clinical Research, Minn., MN;* [4]*Univ Washington, Seattle, WA.*

Low serum magnesium (Mg) level has been associated with increased risk of diabetes mellitus, hypertension, and cardiovascular diseases in the general population. Prior observational studies have shown hypomagnesemia was associated with increased all-cause mortality in hemodialysis (HD) patients. However, these studies were limited by short follow-up, failure to account for Mg changes over time, and lack of generalizability to the US population. We hypothesize that low serum Mg is associated with increased risk of death.

In a US cohort of 9,359 HD patients who initiated dialysis between 2007-2011, we examined the association of serum Mg with all-cause mortality using multivariable adjusted time-varying Cox proportional hazards models. After a follow-up of 19 ±15 (mean ±SD) months, 2,636 deaths occurred. Compared to serum Mg 2.2-<2.4 mg/dl (ref.), patients with Mg <2 mg/dl had a significantly higher risk of all-cause mortality over time after adjustment for baseline characteristics and co-morbidities. Associations were attenuated to the null after additional adjustments for other routine laboratory measurements especially serum albumin. Among patients with low albumin <3.5 g/dl (n=4,066), low Mg <2 mg/dl (vs. Mg ≥2 mg/dl) was associated with additional 17% higher risk for death (hazard ratio 1.17, 95% CI: 1.05-1.31, p=0.004).



Hence, in a large US cohort of HD patients, lower serum Mg was significantly associated with increased all-cause mortality, especially in patients with low serum albumin. These findings may help identify HD patients with higher mortality risk for potential interventions.

159

IGA NEPHROPATHY PRESENTING DURING PREGNANCY

Kelly Liang and Sheldon Bastacky, University of Pittsburgh, Pittsburgh, PA, USA

Proteinuria and hypertension during pregnancy are often attributed to preeclampsia. However, other glomerular disorders may present with similar signs and symptoms such as proteinuria, hypertension (HTN), microscopic hematuria, and worsening renal function. We report a case of IgA nephropathy diagnosed by renal biopsy after presenting with symptoms suggestive of preeclampsia during pregnancy.

A 32 year old pregnant African American female (G7, P1051) presented with microscopic hematuria and proteinuria, thought possibly related to preeclampsia. She had estimated 2 g/day proteinuria at 3-4 months gestation, but extensive serologic blood tests were unremarkable. She was admitted at 7 months with HTN and nephrotic range proteinuria (4.8 g/day), with presumed superimposed preeclampsia. Her creatinine (Cr) increased from 1.0 to 1.2 to 1.4 mg/dl within a 12-h time span shortly after admission. Her Cr improved and remained stable at 0.9-1.1, and her BP fluctuated (130-160/80-100). She underwent induction of labor and delivered a baby girl at 36-5/7 weeks gestation. Her BP remained normal postpartum. Her Cr peaked at 1.6 postpartum, but then stabilized at 1.2. In follow-up one month later, she was found to have persistent proteinuria and hematuria (urinalysis showed 3+ blood, 3+ protein, 5-10 WBC, 10-15 RBC, and urine protein/Cr ratio 1.9). She was recommended to undergo renal biopsy but was reluctant to have the procedure done. She agreed to renal biopsy 1.5 years later when proteinuria and microscopic hematuria failed to resolve with angiotensin converting enzyme inhibitor (ACE-I) therapy. Renal biopsy showed mild mesangial proliferative glomerulonephritis with one crescent, and immunofluorescence and electron microscopy were consistent with IgA nephropathy. She was treated with fish oil and increased dose of ACE-I. Proteinuria improved to 1-1.5 g/day and Cr remained around 1.2-1.3.

This case underscores the importance of close follow-up after delivery in cases of proteinuria and microscopic hematuria that presents during pregnancy, even if presumed to be preeclampsia. Clinicians should pursue renal biopsy for definitive diagnosis of glomerular disorders such as IgA nephropathy in these cases.

160

TRIFERIC DOES NOT INDUCE OXIDATIVE STRESS IN CKD-HD: THE PRIME STUDY

Vivian Lin, Alp T Ikizler, Carrie Guss, Raymond D. Pratt and Ajay Gupta. Rockwell Medical Inc, Michigan, USA and Vanderbilt University, Tennessee, USA.

Iron-carbohydrate complexes administered intravenously generate redox-active non-transferrin-bound iron (NTBI) and induce oxidative stress in CKD-HD patients. Oxidative stress is associated with cardiovascular morbidity and mortality.

Ferric pyrophosphate citrex (SFP, Triferic™) is a low molecular weight investigational parenteral iron salt devoid of a carbohydrate moiety. The PRIME study randomized 108 iron-replete (baseline ferritin 200-1000 µg/L) CKD-HD patients to Triferic or placebo via dialysate for up to 36 weeks. ESA could be titrated to maintain a target Hgb level and IV iron could be administered for serum ferritin <200 µg/L. In the Triferic group at the end of treatment, prescribed ESA doses were reduced by 35% (p=0.045) and prescribed IV iron by 48% (p=0.049).

Markers of inflammation (interleukin-6 [IL6]) and oxidative stress (malonydialdehyde [MDA], F2-isoprostanes [F2Iso] and isofurans [IsoF]) were measured. Over a single dialysis session, in both treatment groups plasma IL6 increased from pre-dialysis to post-dialysis, whereas MDA and IsoF significantly decreased. Over 36 weeks (Week 1 *vs* Week 36), there were no statistically significant differences between study groups in pre-dialysis IL6, MDA or IsoF levels. However, F2Iso levels increased 0.001 ng/mL in the placebo group vs decreased 0.003 ng/mL in the Triferic group (p = 0.046).

Conclusions**:** Regular administration of Triferic via the dialysate does not promote oxidative stress or inflammation either acutely over the course of a single hemodialysis session or after chronic administration for up to 36 weeks.