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Sodium Zirconium Cyclosilicate (ZS-9) in Chronic Kidney Disease Patients with Hyperkalemia

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RAAS inhibitors (RAASi) have known renoprotective and cardioprotective effects; however, RAASi are limited by hyperkalemia (HK; serum K+≥5.1mEq/L). HK is also common in pts with chronic kidney disease (CKD) who are maintained on RAASi (Renin-angiotension-aldosterone system inhibitors). Current HK therapies (eg, sodium polystyrene sulfonate [SPS], Patiromer) are suboptimal because of gastrointestinal (GI) side effects, drug-drug interactions, uncertain efficacy (SPS) or delayed onset of action (Patiromer). There is an unmet need for an easily administered HK treatment that has a rapid onset and can be predictably used in the outpatient setting, hence avoiding visits to the emergency room or hospitalization. Sodium zirconium cyclosilicate (ZS-9) is an oral, taste-less, sorbitol-free, selective cation trap that selectively binds K+ throughout the GI tract. In 2 large double-blind, placebo-controlled, randomized Phase 3 trials, ZS-9 rapidly normalized and maintained serum K+ in HK pts (ZS-003 [NEJM] and HARMONIZE [JAMA]). Here, we present results of a pre-specified subgroup analysis of outpatients with eGFR <60mL/min/1.73m2 and not on dialysis, pooled from these 2 studies. Pts received ZS-9 three times daily (TID) for initial 48h, followed by once-daily treatment for 12 days (ZS-003) or 28 days (HARMONIZE). Pts with eGFR<60 (range 5-59) mL/min/1.73m2 who received ZS-9 10g for the first 48h were evaluated. Of the 1011 pts in the 2 studies, 739 had an eGFR<60, of whom 281 received ZS-9 10g TID. Median age was 68 yrs, 71% were on RAASi, and mean baseline K+ was 5.5mEq/L. ZS-9 significantly reduced serum K+ to normal (K<5.1) within 2.2 hours among 50% of patients; 84% and 97% of pts normalized by 24h and 48h, respectively; mean K+ at 48h was 4.5mEq/L (95%CI 4.3-4.6mEq/L). ZS-9 was well tolerated and the rate of GI adverse events was similar to placebo. A novel agent, ZS-9, rapidly normalized serum K+ within hours in outpatients with CKD stages 3-5, suggesting ZS-9 has the potential to offer another therapeutic option for patients.

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