ZS-9 MAINTAINS NORMOKALEMIA IN HYPERKALEMIC PATIENTS DESPITE CONTINUING RAAS INHIBITORS: A SUBGROUP ANALYSIS FROM A PHASE 3 MULTICENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

Oral Contributions
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Background: Hyperkalemia (HK) frequently develops in patients (pts) with heart failure or chronic kidney disease treated with RAAS inhibitors (RAASi). Continuation of these cardiorenal protective agents is desirable but limited by HK. Sodium zirconium cyclosilicate (ZS-9), a nonabsorbed cation exchanger that specifically traps K+ in the GI tract, acutely restored and maintained normokalemia in HK pts in a Phase 3 study. In this subgroup analysis, we evaluated whether once daily (QD) ZS-9 could prevent hyperkalemia in pts on RAASi therapies.

Methods: This phase 3 study enrolled 753 pts with serum K+ 5.0-6.5 mEq/L who were initially randomized to thrice daily ZS-9 or placebo for 48hrs. Of these, 166 pts who had normalized K+ and were on RAASi were randomized to QD ZS-9 at 5 or 10 g, or PBO for 2 weeks of maintenance therapy. Per protocol, RAASi dose was continued unchanged for the duration of the study. Unpaired t-tests were used to compare K+ between the two groups.

Results: Baseline K+ following normalization was similar in the ZS-9 and PBO groups (4.55 mEq/L and 4.64 mEq/L, respectively). Pts on ZS-9 maintained normokalemia (4.67 mEq/L), whereas those receiving PBO trended back to hyperkalemia by Day 15 (5.06 mEq/L; p<0.05). (Figure).

Conclusion: In pts on RAASi, ZS-9 effectively prevented hyperkalemia compared with placebo, indicating that this novel K+-lowering agent may facilitate continued use of the cardioprotective RAASi by effectively maintaining normokalemia.