005. Patiromer to Enable Spironolactone in Patients with Resistant Hypertension and Chronic Kidney Disease (AMBER): Results in the Prespecified Subgroup with Diabetes

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Purpose: Spironolactone (SPIRO) reduces BP in patients with resistant hypertension (RHTN); however, its use in patients with advanced chronic kidney disease (CKD) is often limited by hyperkalemia. In AMBER, patiromer enabled more persistent use of SPIRO in patients with RHTN and CKD. As SPIRO is recommended in RHTN, and diabetes mellitus (DM) increases hyperkalemia risk, we report results in prespecified subgroups with Type 1 or 2 DM and without DM.

Method: AMBER was a randomized, double-blind, placebo (PBO)-controlled trial in adults with RHTN and eGFR 25 to â‰¤45 mL/min/1.73mÂ². Patients were assigned (1:1) to PBO or patiromer at a starting dose of 8.4 g once daily, and SPIRO 25 mg once daily. Dose titrations were permitted after 1 week for patiromer/PBO to address hyperkalemia or hypokalemia: upward adjustment to 16.8g QD, and then 25.2g QD for local laboratory serum K+ >5.1 mEq/L, and downward adjustment for serum K+ <4.0 mEq/L. Dose of SPIRO was increased to 50 mg QD at week 3 in patients with serum K+ â‰¤5.1 mEq/L if systolic AOBP remained â‰¥120 mmHg. The primary endpoint (between-group difference at Week 12 in the percent of patients on SPIRO) was assessed prospectively in prespecified subgroups by DM status.

Results: 295 patients were randomized, 145 (49%) with DM and 150 (51%) without DM. Baseline mean (SD) serum K+ (mEq/L) was 4.76 (0.34) in patients with DM and 4.67 (0.39) in patients without DM. Significantly more patients treated with patiromer than with PBO remained on SPIRO at Week 12. In the subgroup with DM, 83.6% of patients receiving patiromer remained on SPIRO at week 12 compared with 65.3% of patients receiving PBO (between-group absolute difference=18.3%, 95% confidence interval [CI] 4.4âˆ’32.2; P=0.0111). In the subgroup without DM, 87.8% of patients receiving patiromer remained on SPIRO at week 12, compared with 67.1% of patients receiving PBO (between-group absolute difference=20.7%, 95% CI 7.8âˆ’33.7; P=0.0024). The least squares mean (SE) cumulative SPIRO dose in both subgroups was higher with patiromer than PBO, by 438.7 (177.7) mg in the subgroup with DM and 317.8 (175.0) mg in the subgroup without DM. Adverse events occurred in 61% (PBO) and 60% (patiromer) of patients with DM and in 46% (PBO) and 51% (patiromer) of patients without DM. Four patients had serum magnesium <1.4 mg/dL between baseline and Week 12 (none <1.2 mg/dL), including 3 with DM (1 PBO, 2 patiromer) and 1 without DM (patiromer) patients. In 2 of these patients with DM, serum magnesium was below the lower limit of normal (LLN; 1.8 mg/dL) at baseline. None of these patients had cardiac arrhythmias temporally associated with low magnesium levels, neuromuscular abnormalities, or serum K+ below the LLN (3.5 mEq/L).

Conclusion: Patiromer enabled more patients with advanced CKD and RHTN to continue treatment with SPIRO, regardless of DM status.