Patiromer increased the time to first recurrent HK event vs placebo in patients with T2DM. Through week 8 of the withdrawal phase, significantly ($P < .001$) more T2DM patients on placebo (62%) vs patiromer (19%) had at least 1 recurrent HK event.

Patiromer was well tolerated in patients with T2DM, with mild-to-moderate constipation being the most common adverse event (13% in Part A, 6% in Part B).

For patients with CKD, T2DM, and HK who are taking RAASis, patiromer may provide an option for HK management.

## REPRISE 3b Study in Enrollment Phase

Written by Maria Vinall

The Efficacy and Safety of Tolvaptan in Subjects With Chronic Kidney Disease Between Late Stage 2 to Early Stage 4 Due to Autosomal Dominant Polycystic Kidney Disease [REPRISE 3b; NCT02160145] study is a multinational, phase 3b, randomized-withdrawal, placebo-controlled, double-blind, parallel-group trial. It is currently enrolling patients in 22 countries and expanding. The objective of the trial is to compare the efficacy of tolvaptan, a selective arginine vasopressin $V_2$ receptor antagonist, with placebo in adults with autosomal dominant polycystic kidney disease (ADPKD). Vicente E. Torres, MD, PhD, Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, United States, presented the REPRISE study design in a poster session.

ADPKD is the most common inherited kidney disease in adults and is the fourth-leading cause of end-stage renal disease. It affects approximately 1 in 2500 adults in Europe and the United States. The Tolvaptan Phase 3 Efficacy and Safety Study in ADPKD [TEMPO3/4; NCT00428948] demonstrated the efficacy of tolvaptan to slow the increase in total kidney volume and the decline in kidney function over a 3-year period in subjects with chronic kidney disease (CKD) stage 1 to 3 due to ADPKD [Torres VE et al. *N Engl J Med.* 2012]. Currently, tolvaptan is only approved in Japan for the treatment of patients with ADPKD and rapidly progressive disease.

The REPRISE trial plans to enroll approximately 1300 tolvaptan-naïve ADPKD patients with CKD in late stage 2 to early stage 4. Subjects will be randomized to receive either tolvaptan or placebo for 13.5 months. Subjects may be randomly switched back and forth between treatments (to establish tolerance) at different times for defined intervals and are eligible for open enrollment after the end of the study. Men and women aged 18 to 55 years with an estimated glomerular filtration rate (eGFR) between 25 and 65 mL/min/1.73 $m^2$ or aged 55 to <66 years with an eGFR between 25 and 44 mL/min/1.73 $m^2$ are eligible for the enrollment. Diagnosis of ADPKD is performed with the modified Pei-Ravine criteria including age and number of renal cysts in patients both with and without a family history. Patients with hepatic impairment or liver function abnormalities other than those associated with ADPKD, advanced diabetes, or other significant renal issues (kidney cancer, surgery, or injury) are not eligible to participate.

The primary purpose is to compare the efficacy of tolvaptan with placebo in reducing the change in eGFR from pretreatment (baseline) to post-treatment follow-up. Secondary objectives are to compare tolvaptan to placebo in reducing the decline of annualized eGFR slope, overall and hepatic safety (monthly monitoring of liver abnormalities), and the incidence of ADPKD complications. It is expected that outcomes will support the previous TEMPO findings that tolvaptan is successful in slowing cyst growth and deterioration of kidney function in ADPKD patients in stages 1 to 3. One caution noted was the higher levels of transaminase (>3 times the upper level of normal) in the TEMPO trial. Close monitoring of transaminase will be performed in the current study. Screening for the REPRISE trial began on May 21, 2014.

It is hoped that this trial will not only confirm previous findings, but will also extend understanding of the safety and efficacy of tolvaptan to later stage (3b and 4) CKD.