AMBER STUDY

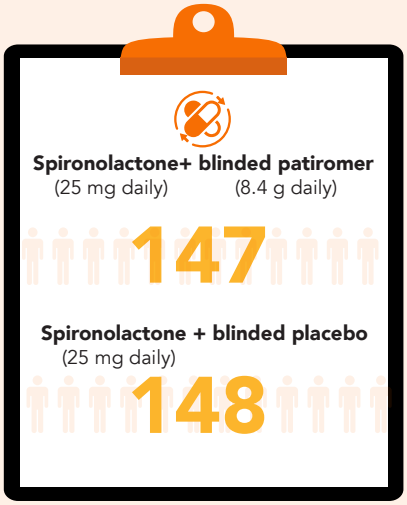
Evaluating whether patiromer can enable persistent use of spironolactone in patients with rHTN and advanced CKD, by managing hyperkalaemia

Spironolactone is an effective treatment for rHTN*, but many previous studies have excluded patients with advanced CKD (eGFR <45 mL/min/1.73 m^2) who are at high risk of hyperkalaemia;[1] **AMBER** is the first study to evaluate whether patiromer can enable spironolactone use in this patient population.

*rHTN: blood pressure above goal despite adherence to a combination of at least 3 optimally dosed antihypertensive medications, one of which is a diuretic

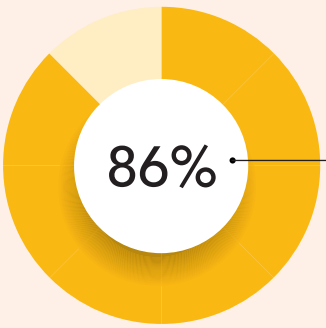
295 patients with **rHTN** and advanced **CKD**
- Systolic AOBP 135–160 mmHg
- eGFR 25–45 mL/min/1.73 m^2

randomised 1:1 to

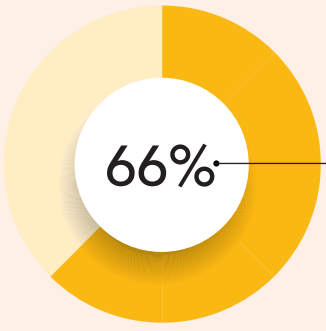


PRIMARY ENDPOINT

In advanced CKD with rHTN, patiromer enables more persistent use of spironolactone
Primary endpoint: between-group difference in % of patients who remained on spironolactone at week 12:

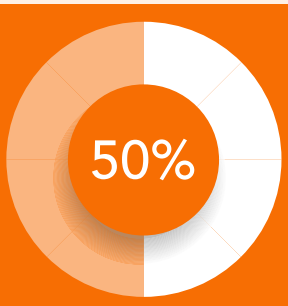


PATIROMER



PLACEBO

Among patients receiving placebo,
2 out of 3 developed hyperkalaemia.



Patiromer reduced this **risk by half.**

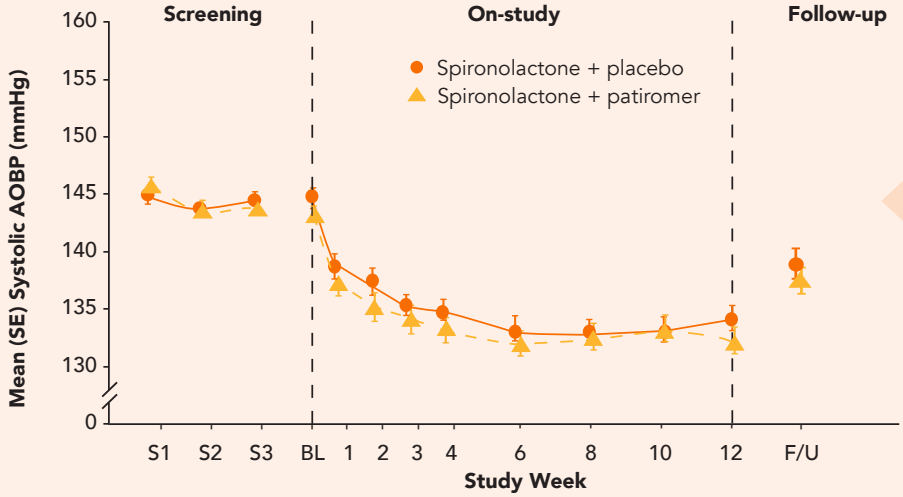
AMBER STUDY

SECONDARY ENDPOINT

Secondary endpoint: between-group difference in change of systolic BP at **week 12**

Spironolactone use in patients with advanced CKD and rHTN resulted in a clinically significant 11–12 mmHg reduction in systolic BP, with a difference between groups of –1 mmHg, P=0.58

SYSTOLIC AOBP OVER TIME



Spironolactone metabolites were detectable long after discontinuation* and with the long half-lives of spironolactone metabolites, approximately half of the systolic BP effect was still present, 2 weeks after discontinuation of spironolactone.

As most discontinuations in the placebo group occurred after 6 weeks of the study; it may be possible that there was insufficient time to observe a difference in systolic AOBP between treatment groups.

* in 36.4% of patients 3 weeks after discontinuation of spironolactone

These findings are noteworthy because meta-analyses of RCTs have shown that a 10 mmHg drop in systolic blood pressure could mean[2,3]

↓ 20%	↓ 20%	↓ 40%	↓ 10–15%	↓ 35%
major CV events	coronary events	heart failure	all-cause mortality	stroke

Patiromer's safety profile was consistent with previous reports[4–6]

Abbreviations: AOBP, automated office blood pressure; BL, baseline; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; F/U, follow-up; RCT, randomised controlled trial; rHTN, resistant hypertension; SE, standard error

1. Agarwal et al. Patiromer versus Placebo to Enable Spironolactone Use in Patients with Resistant Hypertension and Chronic Kidney Disease (AMBER): a Phase 2, Randomised, Double-blind, Placebo-controlled Trial Lancet 2019;394:1540–50.
2. Ettehad D *et al.* Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet* 2016;387:957–967.
3. Thomopoulos C *et al.* Effects of blood pressure lowering on outcome incidence in hypertension. 1.Overview, meta-analyses, and meta-regression analyses of randomized trials. *J Hypertens* 2014;32:2285–2295.
4. Weir MR *et al.* Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N Engl J Med* 2015;372:211–221.
5. Bakris GL *et al.* Effect of patiromer on potassium level in patients with hyperkalemia and diabetic kidney disease: the AMETHYST-DN randomized clinical trial. *JAMA* 2015;314:151–161.
6. Pitt B *et al.* Evaluation of the efficacy and safety of RLY5016, a polymeric potassium binder, in a double-blind, placebo-controlled study in patients with chronic heart failure (the PEARL-HF) trial. *Eur Heart J* 2011;32:820–828.

HQ-PAT-1900147 | Last update: December 2019

VIFOR PHARMA