Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Agarwal R, Rossignol P, Garza D, et al. Patiromer to enable spironolactone use in the treatment of patients with resistant hypertension and chronic kidney disease: rationale and design of the AMBER study.

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Supplemental Table 1. AMBER inclusion criteria.

Category	Inclusion Criteria
Age	≥18 years
Antihypertensive Use	Eligible patients will be taking ≥3 antihypertensive medications at stable doses for ≥28 days; one agent must be a diuretic, and the regimen should also include an ACEI or ARB unless previously not tolerated or contraindicated
Cardiovascular	A systolic AOBP of 135–160 mmHg at the screening visit is required to document that hypertension remains uncontrolled; however, AOBP may be <135 mmHg either at the S2 or S3 visit (but not both)
Renal	Eligibility requires an eGFR of 25–45 mL/min/1.73 m^2 calculated as the mean of two values measured at the S1 and S3 screening visits (or measured 7 to 28 days apart during the screening and run-in period) using the CKD-EPI formula
Serum Potassium	Serum K^+ levels must be 4.3–5.1 mEq/L, as determined by the local laboratory at each of the S1, S3, and S4 visits
Other	All patients must provide written informed consent prior to participation in the study Women of childbearing potential must have a negative serum pregnancy test and agree to use medically acceptable contraception from 28 days before screening until 28 days after study completion

ACEI, angiotensin-converting enzyme inhibitor; AOBP, automated office blood pressure; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CKD-EPI, CKD Epidemiology Collaboration

Supplemental Table 2. AMBER exclusion criteria.

Category	Exclusion Criteria
Cardiovascular	History of untreated secondary causes of hypertension other than CKD Screening systolic AOBP >160 mmHg Cardiovascular event within the past 3 months Clinically significant ventricular arrhythmia Atrial fibrillation >100 bpm Any current use of spironolactone or other mineralocorticoid antagonists (e.g., eplerenone)
Renal	Change in renal function requiring hospitalization or dialysis within 3 months before screening Renal transplant (or anticipated need for renal transplant during the study),
Gastrointestinal	History of bowel obstruction, swallowing disorders, clinically significant gastroparesis, severe gastrointestinal disorders or major gastrointestinal surgery (e.g., large bowel resection)
Potassium-altering medications	Previous use of patiromer in a clinical study Any of the following if doses not stable for at least 28 days prior to screening: Bronchodilators, theophylline, heparin, canagliflozin
Other medications	Use of any investigational product within 30 days or 5 half-lives, whichever is longer, prior to screening Any of the following within 7 days prior to screening: Calcium acetate or calcium carbonate supplements (unless for occasional antacid use, at the discretion of the Investigator), digoxin, direct renin inhibitors (e.g., aliskiren), lanthanum carbonate, lithium, sevelamer, quinidine, sodium polystyrene sulfonate or calcium polystyrene sulfonate, colesevelam, colestipol, cholestyramine, drospirenone, potassium supplements, bicarbonate or baking soda (unless for occasional antacid use, at the discretion of the Investigator), triamterene, amiloride, trimethoprim, tacrolimus, cyclosporine, systemic glucocorticoids, NSAIDs or COX-2 inhibitors (with the exception of low dose aspirin), sympathomimetics
Compliance	Inability to measure blood pressure Clinical history of noncompliance with antihypertensive medications
Other	History of malignancy within the past 12 months except for cured non-melanoma skin cancer Alcohol or drug abuse within the past year

AOBP, automated office blood pressure; BP, blood pressure; CKD, chronic kidney disease; COX, cyclooxygenase; NSAID, nonsteroidal anti-inflammatory drug

Supplemental Table 3. Prohibited medications.

Category	Prohibited medications
Antihypertensive	Prohibited at screening and throughout the study: Eplerenone, or other mineralocorticoid receptor antagonists Aliskiren Potassium sparing diuretics such as triamterene and amiloride No new antihypertensives will be initiated during the study, and doses of baseline antihypertensives will not be changed, with the following exceptions: Patients on spironolactone 50 mg QD with persistent systolic AOBP ≥165 mmHg Patients who discontinued spironolactone and have persistent systolic AOBP ≥165 mmHg Patients with systolic AOBP ≥200 mmHg
Cardiovascular	Digoxin, quinidine, colesevalam, colestipol, cholestyramine, sympathomimetics
Electrolyte modifying	Calcium acetate, calcium carbonate, therapeutic potassium supplements, bicarbonate, baking soda, lanthanum carbonate, sevelamer, sodium polystyrene sulfonate, calcium polystyrene sulfonate
Immunosuppressant	Tacrolimus, cyclosporine, systemic glucocorticoids
Other	Drospirenone, trimethoprim, lithium, NSAIDs or COX-2 inhibitors (except low dose aspirin)

AOBP, automated office blood pressure; COX, cyclooxygenase; NSAID, nonsteroidal anti-inflammatory drug; QD, once-daily