Abstract: P450

A multicenter, randomized, parallel-group pilot study of patiromer in optimizing mineralocorticoid receptor antagonist therapy in hyperkalemic heart failure patients (CONTINUE-HF): study design

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Background/Aims:
Mineralocorticoid receptor antagonists (MRAs), e.g. eplerenone and spironolactone, are recommended in heart failure (HF) guidelines for reduction of morbidity and mortality in HF patients with reduced ejection fraction (HFrEF). However, as inhibitors of the renin–angiotensin–aldosterone system (RAAS), MRAs can induce hyperkalemia (HK), especially in patients with renal dysfunction, and are frequently discontinued or underdosed due to hyperkalemia concerns.

Patiromer is a new potassium-binder using calcium as a counterion exchange. The CONTINUE-HF study (EudraCT number 2017-003555-35) will evaluate, if patiromer added to standard treatment (including MRA) in hyperkalemic HFrEF patients will enable more patients to continue or achieve the guideline recommended target MRA dose compared to standard of care (SoC).

Methods:
This is a multicenter, randomized, prospective, open-label, controlled, parallel group pilot study of patiromer in HFrEF patients with intended dose reduction or discontinuation of MRA therapy due to hyperkalemia.

The study consists of a screening period (up to 14 days), a 42-day treatment phase and a safety follow-up. Inclusion criteria include HFrEF (EF <40%), NYHA Class II/III, eplerenone or spironolactone therapy, and HK (serum potassium =5.1 mmol/l) that limits ability to maintain or increase MRA dose. Eligible patients are randomized 1:1 to receive patiromer or SoC (potassium dietary restriction, enhanced renal potassium elimination, reduction of potassium-sparing drugs) in addition to the MRA. Patients in both treatment groups receive dietary counselling.

The primary endpoint is the proportion of subjects maintaining or achieving the guideline recommended target MRA dose of 50 mg/day in the patiromer versus the SoC group at D42. Secondary endpoints are Patient Global Assessment (PGA), change in EQ-5D-5L, NYHA class, functional capacity, and eplerenone/spironolactone dosage from baseline over time. Additionally, the proportion of subjects on same or higher MRA dose compared to baseline, the change in HF and kidney related parameters such as NT-proBNP, troponin, and urine albumin/creatinine ratio will be analyzed.

CONTINUE-HF is an ongoing study being conducted across 25 sites in Germany and will randomize approximately 100 subjects stratified based on current MRA therapy (eplerenone or spironolactone) and serum potassium level (=5.1 mmol/l to <5.5 mmol/l or =5.5 mmol/l).

Conclusions:
We anticipate that in CONTINUE-HF the proportion of subjects maintaining or achieving optimal (guideline recommended, maximal tolerated dose) eplerenone/spironolactone dosage in the patiromer group will be larger than in the SoC group. The results of this pilot study could be used to design future studies assessing the beneficial effects of enabling eplerenone/spironolactone in this population.