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MINERALOCORTICOID RECEPTOR ANTAGONISM: NEW OPPORTUNITIES FOR CARDIOVASCULAR RESEARCH

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The steroidal Mineralocorticoid receptor antagonists (MRAs) spironolactone and eplerenone have been shown to be effective in reducing mortality and hospitalizations for heart failure in patients with chronic HFrEF. Their role in patients with HFpEF remains controversial since the overall results of TOPCAT were equivocal. An analysis of geographic differences in TOPCAT have however suggested patients randomized from Russia and the Republic of Georgia did not have the mortality risk associated with prior epidemiological and randomized HFpEF studies and that many patients in these countries did not take assigned study drug. The Spirrit trial funded by the Swedish Heart foundation and the NHLBI is therefore currently randomizing > 3000 patients with a LVEF > 40% to spironolactone or placebo using an open label probe design with CV mortality as the primary endpoint . The steroidal MRA spironolactone has also been shown to be the agent of choice in patients with resistant hypertension (PATHWAY). There are however suggestions that MRAs may have an important role in patients with the metabolic syndrome and hypertension at an earlier stage . The Envoy trial ((n=300) will be evaluating patients with visceral obesity and hypertension and will compare the effectiveness of indapamide to spironolactone on top of amlodipine over a 1 year follow up. The use of the steroidal MRAs however is limited by the risk of hyperkalemia. New non nonsteroidal MRAs with a lower incidence of hyperkalemia than spironolactone are currently being investigated in patients with uncontrolled hypertension and an eGFR ,45-15 ml/min/1.73 m2 (N=240) as well as in patients with Diabetic Nephropathy (Figaro ,n=4000, Fidelio n=6000). The availability of these new nonsteroidal MRAs as well as new safe and effective K+ lowering agents such as Patiromer opens the possibility for the use of MRAs in high risk patients with CKD, Diabetes mellitus, heart failure and or hypertension.

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