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| **Supplementary Material 4. Study Outcomes of MRA treatment in HF patients** |
| **Study** | **Subjects,**  | **Study Design** | **Population** | **Primary Endpoint** | **Clinical Outcome** | **SAE** |
| RALES (23) | 1663 | RCT, spironolactone vs placebo | HF, EF <35% | All-Cause Mortality | Reduced all-cause mortality in Spironolactone group | NS clinical SAEs noted in trial group |
| EMPHASIS-HF (24) | 2737 | RCT, Eplerenone vs placebo | HF, EF<35% | Death from cardiovascular causes or hospitalization for heart failure. | Reduced all-cause mortality in Spironolactone group | Increased in non-severe hyperkalemia in Eplerenone arm |
| ARTS-HF (19) | 1066 | RCT, Finerenone with dosage up titrated vs eplerenone | HFrEF with EF <40%, DM with CKD (GFR>30 cc/min per 1.73 m2), CKD without DM (GFR 30-60 cc/ min per 1.73 m2) | Percentage of individuals with a decrease of >30% in plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) from baseline to Day 90 | Finerenone was well tolerated and induced a 30% or greater decrease in NT-proBNP levels in a similar proportion of patients to eplerenone | Similar rates of Adverse effects across all groups, low rates of renal adverse effects |
| EPHESUS (22) | 6632 | RCT eplerenone vs placebo | Acute myocardial infection of LV function <40% | Death from any cause and death from cardiovascular causes or hospitalization for heart failure, acute myocardial infarction, stroke, or ventricular arrhythmia | Reduction of mortality and morbidity in Eplerenone group | Higher rates of serious and non serious hyperkalemia in Eplerenone group |
| Cicoira et al. (20) | 106 | Spironolactone vs control | Stable CHF | Improvement of LV function and exercise tolerance  | Improvement in LV function and volume with increased dosage | N/A |
| Aldo-DHF (21) | 422 | RCT, spironolactone vs placebo | chronic New York Heart Association class II or III heart failure, preserved left ventricular ejection fraction of 50% or greater, and evidence of diastolic dysfunction. | Changes in diastolic function (E/e') on echocardiography at 12 months. | improved left ventricular diastolic function in Spironolactone group | Increased potassium and lower eGFR values in trial group |

# ﻿Aldo-DHF, Aldosterone receptor blockade in Diastolic Heart Failure; ARTS-HF, Mineralocorticoid Receptor Antagonist Tolerability Study–Heart Failure; EMPHASIS-HF, Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure; EPHESUS, Eplerenone Post–Acute Myocardial Infarction Heart Failure Efficacy and Survival Study; RALES, Randomized Aldactone Evaluation Study; ACE indicates angiotensin-converting enzyme inhibitor; BNP, B-type natriuretic peptide; CHF, congestive heart failure; CKD, chronic kidney disease; Cr, creatinine; DM, diabetes mellitus; EF, ejection fraction; GFR, glomerular filtration rate; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; NA, not applicable; RCT, randomized controlled trial.

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