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| **Supplementary Material 3. Study results of ARB's in patients with HF** |
| **Study** | **Study Size** | **Protocol** | **Primary Endpoint** | **Population** | **Clinical Outcome** | **SAE due to treatment** |
| Val-HeFT (12) | 5010 | RCT, valsartan vs placebo | All-cause mortality | Symptomatic HF, EF <40% | Reduction in HF hospitalization  | Combination of ARB, ACEi and beta blocker showed increased mortality |
| CHARM- Overall (13) | 7599 | RCT, candesartan vs placebo | The primary outcome of the overall program was all-cause mortality, and for all the component trials was cardiovascular death or hospital admission for CHF.  | HF with EF <40% and HF with EF >40% | Significant reduced cardiovascular deaths and hospital admissions for heart failure.  | More discontinuations due to renal function, hypotension, and hyperkalemia. |
| HEAAL (18) | 3846 | High-vs low- dose losartan | The primary endpoint was death or admission for heart failure | Symptomatic HF, EF <40%, intolerance of ACE inhibitor | Losartan150 mg daily reduced the rate of death or admission for heart failure in patients with heart failure, reduced left-ventricular ejection fraction, and intolerance to ACE inhibitor | cases of renal impairment, hypotension, and hyperkalemia in the high-dose group |
| ELITE (14) | 722 | Captopril vs losartan | Tolerability measure of a persisting increase in serum creatinine of 26.5 mumol/L or more (> or = 0.3 mg/dL) on therapy | New York Heart Association (NYHA) class II-IV heart failure and ejection fractions of 40% | Losartan group experienced lower mortality rates | Higher discontinuation rate in captopril group due to cough |
| VALIANT (15) | 14,808 | Valsartan vs Captopril Vs both | All-cause Mortality  | Acute myocardial infarction plus evidence of left ventricular systolic dysfunction | NS difference in mortality between Valsartan and Captopril alone group. Higher mortality in combined group. | Valsartan + captopril group had increased rates of renal impairment, hypotension, and hyperkalemia |
| ONTAR-GET (16) | 25,620 | Telmisartan, Ramipril, or both | Death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure | Coronary, peripheral, or cerebrovascular disease or diabetes with end-organ damage.  | NS difference in clinical benefit derived between groups | More adverse effects in combination group  |
| Heran et al. (17)  | 17,900 | Systemic review of RCTs investigating ARB use | Mortality, morbidity, discontinuation due to ARB use | LVEF ≤40% | ARBs did not reduce total mortality or total morbidity  | Combinations of ARBs plus ACEIs increased the risk of withdrawals due to adverse effects  |

﻿CHARM, Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity; ELITE, Evaluation of Losartan in the Elderly; GFR, glomerular filtration rate; HEAAL, Heart failure Endpoint Evaluation of Angiotensin II Antagonist Losartan; ONTARGET, Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial; VALIANT, Valsartan in Acute Myocardial Infarction; Val-HeFT, Valsartan in Heart Failure. ACE, angiotensin-converting-enzyme; ARB, angiotensin receptor blocker; CHF, Chronic heart failure; CKD, chronic kidney disease; HFrEF, Heart failure with reduced ejection factor; EF, ejection fraction; RCT, randomized control trial; HF, heart failure; NS, not significant; SAE, serious adverse event; SCr, serum creatinine

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