Mineralocorticoid Receptor Antagonists And Race In Heart Failure

An Individual Participant Data Meta-Analysis of Randomized Trials

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Introduction: Race and HF

- Although race is a social construct, Black people have a higher prevalence of HF and worse outcomes than White people
- Differences in renin-angiotensin-aldosterone system (RAS) activity have been consistently reported in Black compared to White people; Black patients may have less blood pressure reduction with RAS inhibitors than non-Black patients
- Concerns have been raised that RAS inhibitors are less effective in Black patients than non-Black patients with HF
- Black individuals are underrepresented in clinical trials, making it difficult to obtain a robust estimate of the effect of a therapy
- We examined the efficacy and safety of MRAs in patients with HF in a *post hoc* individual-participant data meta-analysis of the four large placebo-controlled trials

Overview of MRA trials

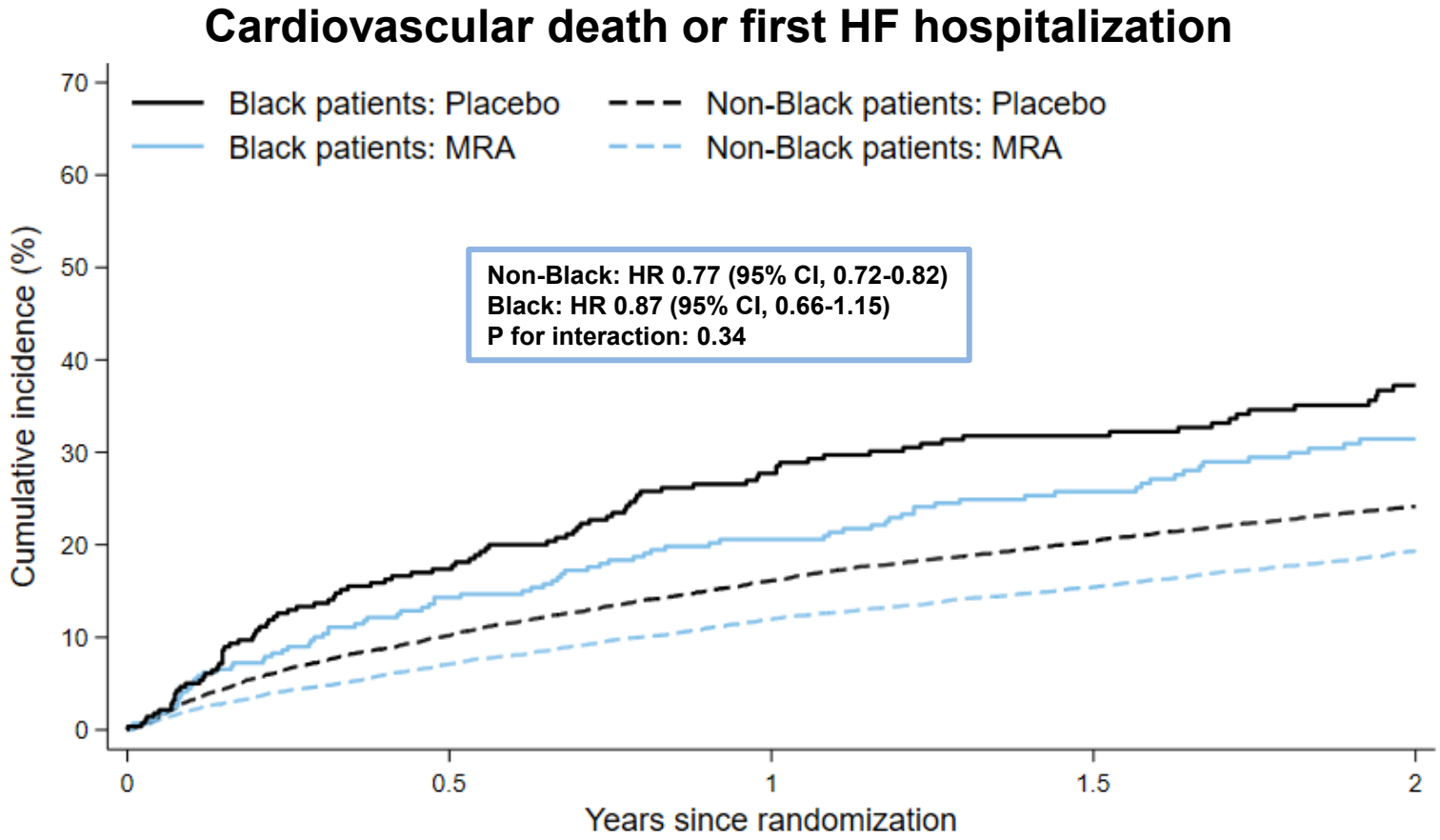
	HFrEF		HFmrEF/HFpEF	
	RALES N=1663	**EMPHASIS-HF N=2737**	**TOPCAT N=3445**	**FINEARTS-HF N=6001**
Inclusion criteria	- LVEF ≤35% - NYHA III-IV - ACEi + diuretic	- LVEF ≤35% - NYHA II - ACEi/ARB + BB	- LVEF ≥45% - Prior HFH or ↑natriuretic peptides	- LVEF ≥40% - NYHA II-IV - Structural heart disease - ↑natriuretic peptides
Exclusion criteria	- Creatinine >2.5 mg/dL - Potassium >5.0 mmol/L	- eGFR <30ml/min/1.73m^2 - Potassium >5.0 mmol/L	- Creatinine ≥2.5 mg/dL - eGFR <25ml/min/1.73m^2 - Potassium ≥5.0 mmol/L	- eGFR <25ml/min/1.73m^2 - Potassium >5.0 mmol/L
Intervention	Spironolactone (sMRA) vs. placebo	Eplerenone (sMRA) vs. placebo	Spironolactone (sMRA) vs. placebo	Finerenone (nsMRA) vs. placebo
Black persons (%)	7.2	2.4	8.8	1.5

13,846 participants; 577 Black persons; median follow-up 30 months
Primary outcome: Cardiovascular death or first HF hospitalization

Selected baseline characteristics by race

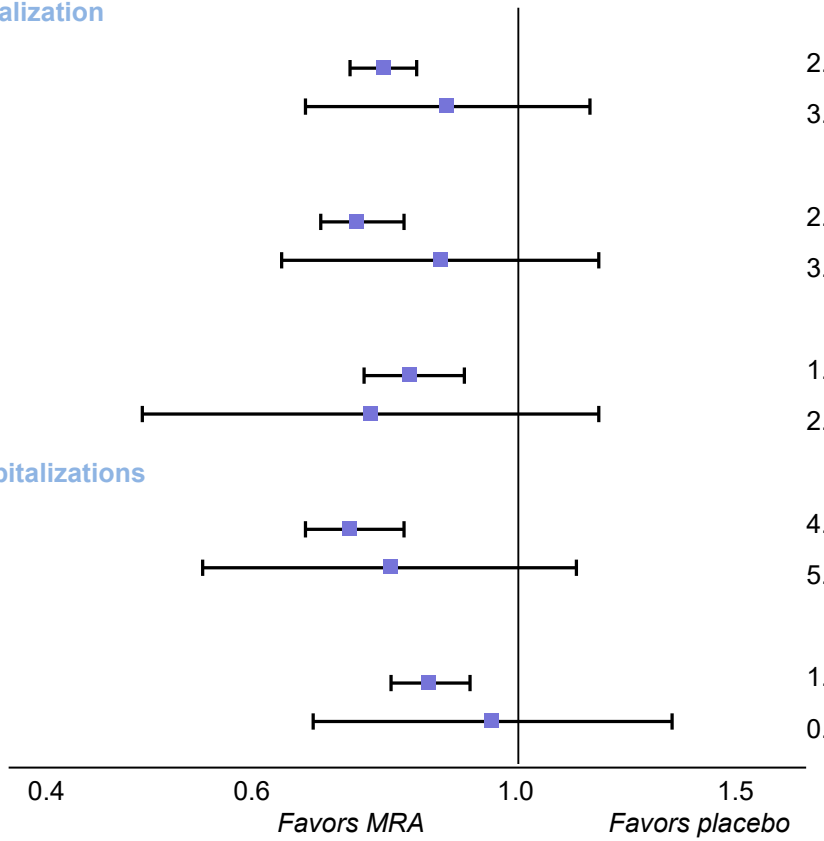
	Non-Black patients	Black patients	P-value
Male sex, %	61	44	<0.001
Age, median	70	64	<0.001
eGFR (mL/min/1.73cm^2), mean	67	63	<0.001
NT-proBNP (pg/mL), median	1014	926	0.55
NYHA class III/IV, %	33	46	<0.001
LVEF >40%, %	67	66	0.85
BMI >30 kg/m^2, %	43	67	<0.001
Hospitalization for HF	62	68	0.011
Type 2 diabetes	34	40	0.004
Hypertension	77	75	0.30
Atrial fibrillation	41	19	<0.001
Myocardial infarction	32	13	<0.001

Effect of MRAs by race: Primary outcome



Effect of MRAs by race: Clinical outcomes

Outcome	Rate difference	HR/RR (95% CI)	P-value for Interaction
CV death or first HF hospitalization			0.34
Non-Black	2.7	0.77 (0.72-0.82)	
Black	3.9	0.87 (0.66-1.15)	
First HF hospitalization			0.36
Non-Black	2.3	0.73 (0.68-0.80)	
Black	3.4	0.86 (0.63-1.17)	
CV death			0.80
Non-Black	1.0	0.81 (0.74-0.90)	
Black	2.0	0.75 (0.48-1.17)	
CV death and total HF hospitalizations			0.85
Non-Black	4.9	0.72 (0.66-0.80)	
Black	5.3	0.78 (0.54-1.12)	
All-cause death			0.46
Non-Black	1.2	0.84 (0.78-0.91)	
Black	0.8	0.95 (0.67-1.35)	



Effect of MRAs by race: Adverse events

% of patients	Non-Black patients		Black patients		
	MRA N=6602	Placebo N=6644	MRA N=295	Placebo N=282	P-value for interaction
Hypotension					
SBP <90 mmHg	5.3	3.6	6.7	3.7	0.51
SBP <100 mmHg	19.0	14.5	24.9	15.1	0.13
Elevated serum creatinine					
≥2.5 mg/dL	5.3	3.2	11.2	10.3	0.18
≥3.0 mg/dL	2.3	1.3	4.3	4.9	0.12
Reduction in eGFR					
>20%	51.0	39.3	59.2	48.4	0.78
>30%	31.0	20.6	41.9	27.4	0.62
Elevated serum potassium					
>5.5 mmol/L	13.6	6.5	10.9	4.8	0.86
>6.0 mmol/L	2.9	1.4	3.5	1.1	0.49
Reduced serum potassium					
<3.5 mmol/L	7.2	13.3	14.4	24.5	0.82

Sensitivity analyses

- Population restricted to those enrolled in Americas
- Non-Black population divided into White, Asian, and other

Conclusions: MRAs in HF according to race

- In a patient-level pooled meta-analysis of ~14,000 participants from four HF trials, MRAs reduced the absolute and relative risk of clinical events to a similar extent in Black and non-Black patients
- The effects of MRAs on experiencing adverse events did not differ meaningfully by race
- The benefits and tolerability of MRAs in HFrEF and HFpEF, individually, were consistent regardless of race