

Supplemental Material

Supplemental Table 1. Comparison of the characteristics of the patients who died or who were lost to follow-up with the whole baseline population

	Baseline	Dead or Lost to Follow-up	P-value
Variables	(N=1325)	(N=276)	
MRA at baseline, n (%)	741 (55.9)	154 (55.8)	0.962
Age, years	66.1 ± 12.2	68.4 ± 11.9	<0.001
Male gender, n (%)	1027 (77.5%)	216 (78.3)	0.737
White caucasian, n (%)	1305 (98.5%)	270 (97.8)	0.309
Southern Europe countries, n (%)	775 (58.5%)	172 (62.3)	0.147
BMI, kg/m ²	27.7 ± 5.5	27.1 ± 5.5	0.06
Heart rate, bpm	83.2 ± 21.7	82.2 ± 19.0	0.38
SBP, mmHg	123 ± 21	119 ± 27	0.002
Pulmonary rales, n (%)	677 (52.4%)	163 (60.8)	0.002
Peripheral edema, n (%)	609 (56.9%)	150 (65.8)	0.002
Elevated JVP, n (%)	293 (31.7%)	76 (41.5)	0.001
NYHA class III/IV, n (%)	797 (61.4%)	184 (68.7)	0.006
Orthopnea, n (%)	439 (33.2%)	112 (40.6)	0.003
LVEF, %	26.2 ± 6.4	25.8 ± 6.9	0.23
Primary HF etiology, n (%)	-		0.003
Ischemic	574 (43.3%)	145 (52.5)	
Hypertensive	106 (8.0%)	24 (8.7)	
Valvular	73 (5.5%)	12 (4.3)	
Other/miscellaneous	572 (43.2%)	95 (34.4)	
Hemoglobin, g/dL	13.5 ± 1.8	12.9 ± 1.8	<0.001
eGFR, ml/min/1.73m ²	66.2 ± 20.7	60.8 ± 19.5	<0.001
eGFR <45 ml/min/1.73m ² , n (%)	224 (16.9%)	71 (25.7)	<0.001
Sodium, mmol/L	139 ± 4	138.6 ± 4.3	<0.001
Potassium, mmol/L	4.2 ± 0.5	4.1 ± 0.5	<0.001
Potassium <4 mmol/L, n (%)	396 (29.9%)	107 (38.8)	0.12
LogNT-pro BNP, ng/L	2.97 ± 1.31	3.45 ± 1.41	<0.001
Hypertension, n (%)	756 (57.1%)	153 (55.4)	0.541
Atrial Fibrillation, n (%)	562 (42.4%)	136 (49.3)	0.010
Diabetes mellitus, n (%)	402 (30.3%)	105 (38.0)	0.002
COPD, n (%)	220 (16.6%)	54 (19.6)	0.137
Stroke, n (%)	119 (9.0%)	33 (12.0)	0.052
PAD, n (%)	123 (9.3%)	35 (12.7)	0.029
Device therapy, n (%)	336 (25.4%)	81 (29.3)	0.087
PCI or CABG, n (%)	411 (31.0%)	105 (38.0)	0.005
Loop diuretic, n (%)	1319 (99.5%)	275 (99.6)	0.801
ACEi/ARB, n (%)	995 (75.1%)	195 (70.7)	0.055
≥50% dose, n (%)*	681 (54.4%)	121 (43.8)	<0.001

Beta-blocker, n (%)	1108 (83.6%)	219 (79.3)	0.031
≥50% dose, n (%)*	455 (36.3%)	73 (26.4)	<0.001
Digoxin, n (%)	250 (18.9%)	62 (22.5)	0.086
Deaths, n (%)	297 (22.4)	169 (61.2)	<0.001

*At V1 the up-titration period was the first 3 months.

Legend: MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure; JVP, jugular venous pressure; NYHA, New York Heart Association; HF, heart failure; eGFR, estimated glomerular filtration rate; NT-pro BNP, n-terminal pro brain natriuretic peptide; COPD, chronic pulmonary obstructive disease; PAD, peripheral artery disease; PCI or CABG, percutaneous coronary intervention or coronary artery bypass grafting; ACEi/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker.

Country location in the BIOSTAT-CHF were considered as follows: Southern Europe: Greece, Italy, France, Serbia, and Slovenia; Northern Europe: Netherlands, Sweden, Norway, Germany, Poland, and United Kingdom.

Supplemental Table 2. Spironolactone or Eplerenone prescription drop out and initiation from baseline to 9 months in the 1049 patients who completed the two visits

	Spironolactone at Baseline n=448 (42.8)	Eplerenone at Baseline n=137 (13.1)	No MRA at Baseline n=461 (44.1)	p-value
Spironolactone at 9 months n=480 (45.9)	367 (81.9)	3 (2.2)	110 (23.9)	<0.001
Eplerenone at 9 months n=182 (17.4)	14 (3.1)	110 (80.3)	58 (12.6)	
No MRA at 9 months n=384 (36.7)	67 (15.0)	24 (17.5)	293 (63.6)	

Legend: MRA, mineralocorticoid receptor antagonist.

The % presented are relative to the total of 1046 patients due to 3 (0.3%) missing values.

Supplemental Table 3. Patterns of MRA prescription relative to the proportion of patients who improved left ventricular ejection fraction above 35% from baseline to 9 months

	LVEF <35% (n=379)	LVEF ≥35% (n=199)	P-value
MRA at both visits	211 (55.7%)	74 (37.2%)	<0.001
MRA only at baseline	21 (5.5%)	18 (9%)	
MRA only at 9 months	57 (15%)	31 (15.6%)	
No MRA	90 (23.7%)	76 (38.2%)	

Legend: LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist.

From the 1049 patients who completed the 2 visits, 578 (55%) had an echo performed at both visits (45% missing values).