

SUPPLEMENTAL MATERIAL

Table S1. Comparison of Baseline Characteristics between Biomarker Cohort and Other ASCEND-HF patients in the Intention to Treat Population.

Characteristic	All Patients (N=7141)	Cardiac Markers Cohort		P-Value
		Excluded (N=6456)	In-Cohort (N=687)	
Patient Characteristics				
Age, yrs (median, 25th-75th)	67 (56-76) [7141]	67 (56-76) [6454]	67 (55-78) [687]	0.41
Female Sex	4697/7141 (65.8%)	4210/6454 (65.2%)	487/687 (70.9%)	0.003
Race				<0.001
White	3989/7140 (55.9%)	3516/6453 (54.5%)	473/687 (68.9%)	
Black	1077/7140 (15.1%)	884/6453 (13.7%)	193/687 (28.1%)	
Asian	1767/7140 (24.7%)	1758/6453 (27.2%)	9/687 (1.3%)	
Other	307/7140 (4.3%)	295/6453 (4.6%)	12/687 (1.7%)	
Region				<0.001
Asia-Pacific	1762/7141 (24.7%)	1761/6454 (27.3%)	1/687 (0.1%)	
Central Europe	967/7141 (13.5%)	936/6454 (14.5%)	31/687 (4.5%)	
Latin America	665/7141 (9.3%)	647/6454 (10.0%)	18/687 (2.6%)	
North America	3243/7141 (45.4%)	2635/6454 (40.8%)	608/687 (88.5%)	
Western Europe	504/7141 (7.1%)	475/6454 (7.4%)	29/687 (4.2%)	
BMI, kg/m ² (median, 25th-75th)	28 (24-33) [7077]	27 (24-32) [6391]	30 (26-36) [686]	<0.001
Weight, kg (median, 25th-75th)	78 (64-95) [7139]	77 (64-93) [6452]	89 (74-107) [687]	<0.001
Systolic BP, mmHg (median, 25th-75th)	123 (110-140) [7141]	123 (110-140) [6454]	125 (111-140) [687]	0.30
Diastolic BP, mmHg (median, 25th-75th)	74 (66-83) [7140]	75 (67-83) [6454]	72 (64-83) [686]	0.005
Heart Rate, bpm (median, 25th-75th)	82 (72-95) [7140]	82 (72-95) [6453]	78 (70-89) [687]	<0.001
Smoking Status				<0.001
Current Smoker	963/7138 (13.5%)	865/6451 (13.4%)	98/687 (14.3%)	
Former Smoker	2537/7138 (35.5%)	2221/6451 (34.4%)	316/687 (46.0%)	
Never Smoker	3638/7138 (51.0%)	3365/6451 (52.2%)	273/687 (39.7%)	
Alcohol Use	641/7142 (9.0%)	560/6455 (8.7%)	81/687 (11.8%)	0.007
Patient Status				
HF Hospitalization within prior year	2785/7134 (39.0%)	2502/6448 (38.8%)	283/686 (41.3%)	0.21
Ischemic Etiology	4293/7140 (60.1%)	3869/6453 (60.0%)	424/687 (61.7%)	0.37
Ejection Fraction, % (median, 25th-75th)	30 (20-37) [5477]	30 (20-36) [4920]	26 (20-40) [557]	0.023
EF ≥= 50	661/5477 (12.1%)	574/4920 (11.7%)	87/557 (15.6%)	0.007
Trop I > ULN	635/2672 (23.8%)	557/2333 (23.9%)	78/339 (23.0%)	0.73

Characteristic	Cardiac Markers Cohort			P-Value
	All Patients (N=7141)	Excluded (N=6456)	In-Cohort (N=687)	
NYHA Class				0.002
I	255/5893 (4.3%)	225/5401 (4.2%)	30/492 (6.1%)	
II	1098/5893 (18.6%)	989/5401 (18.3%)	109/492 (22.2%)	
III	2853/5893 (48.4%)	2610/5401 (48.3%)	243/492 (49.4%)	
IV	1687/5893 (28.6%)	1577/5401 (29.2%)	110/492 (22.4%)	
Hx of Myocardial Infarction	2490/7140 (34.9%)	2240/6453 (34.7%)	250/687 (36.4%)	0.38
Patient History				
Hx of Hypertension	5150/7141 (72.1%)	4613/6454 (71.5%)	537/687 (78.2%)	<0.001
Hx of Diabetes	3046/7141 (42.7%)	2714/6454 (42.1%)	332/687 (48.3%)	0.002
Atrial Fibrillation or Flutter	2674/7141 (37.4%)	2396/6454 (37.1%)	278/687 (40.5%)	0.085
Ventricular Tachycardia	638/7141 (8.9%)	541/6454 (8.4%)	97/687 (14.1%)	<0.001
Hx of Hyperlipidemia	2985/7140 (41.8%)	2538/6453 (39.3%)	447/687 (65.1%)	<0.001
Hx of Cerebrovascular Dz (incl Stroke)	842/7141 (11.8%)	740/6454 (11.5%)	102/687 (14.8%)	0.009
Hx of PVD	740/7141 (10.4%)	664/6454 (10.3%)	76/687 (11.1%)	0.53
Hx of Chronic Respiratory Disease (incl COPD)	1178/7140 (16.5%)	1015/6454 (15.7%)	163/686 (23.8%)	<0.001
Prior Valve Surgery	333/7143 (4.7%)	297/6456 (4.6%)	36/687 (5.2%)	0.45
Prior PCI	1169/7133 (16.4%)	1016/6448 (15.8%)	153/685 (22.3%)	<0.001
Prior CABG	1316/7141 (18.4%)	1121/6454 (17.4%)	195/687 (28.4%)	<0.001
Coronary Artery Disease	3904/7139 (54.7%)	3495/6452 (54.2%)	409/687 (59.5%)	0.007
Cancer within the prior 5 years	272/7141 (3.8%)	236/6454 (3.7%)	36/687 (5.2%)	0.039
Chronic Liver Disease	190/7141 (2.7%)	169/6454 (2.6%)	21/687 (3.1%)	0.50
Hx Dialysis	75/7141 (1.1%)	61/6454 (0.9%)	14/687 (2.0%)	0.008
Patient Labs				
Sodium, mmol/L (median, 25th-75th)	139 (136-141) [6682]	139 (136-141) [6028]	139 (136-141) [654]	0.11
Creatinine, mg/dL (median, 25th-75th)	1.2 (1.0-1.6) [6762]	1.2 (1.0-1.6) [6101]	1.3 (1.0-1.7) [661]	<0.001
Blood Urea Nitrogen, mg/dL (median, 25th-75th)	25 (18-39) [6595]	26 (18-39) [5942]	24 (18-35) [653]	0.034
HGB, g/dL (median, 25th-75th)	12.7 (11.3-14.0) [6592]	12.7 (11.3-14.1) [5936]	12.5 (11.1-13.7) [656]	<0.001
Patient Meds - Pre-Randomization				
ACE-i or ARB	4340/7139 (60.8%)	3905/6452 (60.5%)	435/687 (63.3%)	0.15
Beta Blocker	4158/7139 (58.2%)	3633/6452 (56.3%)	525/687 (76.4%)	<0.001

Characteristic	Cardiac Markers Cohort			P-Value
	All Patients (N=7141)	Excluded (N=6456)	In-Cohort (N=687)	
Aldosterone Antagonists	1992/7140 (27.9%)	1827/6453 (28.3%)	165/687 (24.0%)	0.017
Oral or Topical Nitrates	1681/7140 (23.5%)	1511/6453 (23.4%)	170/687 (24.7%)	0.44
Digoxin or Digitalis Glycoside	1895/7139 (26.5%)	1756/6452 (27.2%)	139/687 (20.2%)	<0.001
Hydralazine	532/7140 (7.5%)	434/6453 (6.7%)	98/687 (14.3%)	<0.001
Calcium Channel Blocker	923/7140 (12.9%)	816/6453 (12.6%)	107/687 (15.6%)	0.030
Aspirin	3507/7140 (49.1%)	3103/6453 (48.1%)	404/687 (58.8%)	<0.001
Loop Diuretic	6788/7138 (95.1%)	6116/6451 (94.8%)	672/687 (97.8%)	<0.001
Clopidogrel	1142/7140 (16.0%)	1036/6453 (16.1%)	106/687 (15.4%)	0.67
Anticoagulant	1722/7140 (24.1%)	1491/6453 (23.1%)	231/687 (33.6%)	<0.001
Patient Implant/Rhythm				
Implantable Cardioverter Defibrillator	1163/7141 (16.3%)	946/6454 (14.7%)	217/687 (31.6%)	<0.001
Biventricular Pacemaker (CRT)	640/7141 (9.0%)	523/6454 (8.1%)	117/687 (17.0%)	<0.001
Pacemaker	440/7141 (6.2%)	395/6454 (6.1%)	45/687 (6.6%)	0.66
Patient Quality of Life				
EQ5D -VAS (median, 25th-75th)	0.60 (0.33-0.78) [6771]	0.60 (0.33-0.78) [6105]	0.71 (0.51-0.82) [666]	<0.001
Depression treated with Meds	562/7141 (7.9%)	458/6454 (7.1%)	104/687 (15.1%)	<0.001
Patient Biomarkers				
NTproBNP, pg/mL (median, 25th-75th) [n]	4501 (2098-9177) [3817]	4540 (2110-9200) [3587]	3801 (1875-8117) [230]	
BNP, pg/mL (median, 25th-75th) [n]	990 (544-1850) [2632]	977 (528-1830) [2206]	1115 (633-1923) [426]	
Baseline NTproBNP, from biomarker data	5791 (3011-11971) [687]	. (-.) [0]	5791 (3011-11971) [687]	
NTproBNP at 48-72 Hours, from biomarker data	3029 (1187-6645) [684]	. (-.) [0]	3029 (1187-6645) [684]	
Change in NTproBNP at 48-72h, from biomarker data	-2182 (-5468--725) [684]	. (-.) [0]	-2182 (-5468--725) [684]	
Symptoms at Randomization				
Dyspnea				<0.001
At Rest	4415/7140 (61.8%)	4031/6453 (62.5%)	384/687 (55.9%)	
With Minimal Activity	2725/7140 (38.2%)	2422/6453 (37.5%)	303/687 (44.1%)	
Orthopnea	5485/7132 (76.9%)	4925/6445 (76.4%)	560/687 (81.5%)	0.003
Nocturnal Dyspnea	4449/7126 (62.4%)	4029/6439 (62.6%)	420/687 (61.1%)	0.46
Weight Gain	4673/7118 (65.7%)	4168/6432 (64.8%)	505/686 (73.6%)	<0.001

Characteristic	Cardiac Markers Cohort			P-Value
	All Patients (N=7141)	Excluded (N=6456)	In-Cohort (N=687)	
Pulmonary Congestion / Edema w rales/crackles	6201/7136 (86.9%)	5655/6449 (87.7%)	546/687 (79.5%)	<0.001
X-ray indicating pulm cong	5206/6419 (81.1%)	4714/5768 (81.7%)	492/651 (75.6%)	<0.001
Peripheral Edema	5330/7140 (74.6%)	4775/6453 (74.0%)	555/687 (80.8%)	<0.001
Elevated JVP	4003/7136 (56.1%)	3589/6449 (55.7%)	414/687 (60.3%)	0.021
S3 Gallop	1668/7136 (23.4%)	1514/6449 (23.5%)	154/687 (22.4%)	0.53
MV Regurg	1927/7136 (27.0%)	1754/6449 (27.2%)	173/687 (25.2%)	0.26

Abbreviations:

BMI = body mass index

BP = blood pressure

HF = heart failure

EF= ejection fraction

Trop I = troponin I

ULN = upper limit of normal

NYHA = New York Heart Association

PVD = peripheral vascular disease

PCI – percutaneous coronary intervention

CABG = coronary artery bypass grafting

HGB= hemoglobin

ACEI = angiotensin converting enzyme inhibitor

ARB = angiotensin receptor blocker

EQ5D = EuroQol-5 Dimensions survey

VAS = Visual Analog scale

JVP = jugular venous pulsation

MV = mitral valve

Table S2. Event Rates by Obesity Class.

Outcomes	Obesity Class				
	Overall (N=686)	Non- Obese (N=346)	Class I (N=147)	Class II (N=86)	Class III (N=107)
30-Day Death or HF-Rehosp.	86	42	17	9	18
30-Day Death or All Cause- Rehosp.	141	73	26	12	30
Worsening Renal Function	65	29	11	13	12
180-Day Death	78	53	9	7	9