Supplementary Online Content

Felker GM, Solomon SD, Claggett B, et al. Assessment of omecamtiv mecarbil for the treatment of patients with severe heart failure: a post hoc analysis of data from the GALACTIC-HF randomized clinical trial. *JAMA Cardiol*. Published online October 13, 2021. doi:10.1001/jamacardio.2021.4027

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Baseline Characteristics by Severe Heart Failure Status

	Severe HF	Not Severe HF	
	n=2258	n=5974	
Demographics			
Age - yr	64.5 ± 11.6	64.5 ± 11.3	p=0.75
Sex, Female	477 (21.1%)	1272 (21.3%)	p=0.87
Race			p<0.001
Asian	153 (6.8 %)	557 (9.3 %)	
Black	177 (7.8 %)	385 (6.4 %)	
Other	129 (5.7 %)	434 (7.3 %)	
White	1799 (79.7%)	4598 (77.0%)	
Geographic Region			p<0.001
Asia	141 (6.2 %)	529 (8.9 %)	
Eastern Europe/Russia	810 (35.9%)	1871 (31.3%)	
Latin America	324 (14.3%)	1250 (20.9%)	
US And Canada	434 (19.2%)	952 (15.9%)	
Western Europe/South Africa/Australasia	549 (24.3%)	1372 (23.0%)	
Randomization Setting: In-patient	937 (41.5%)	1147 (19.2%)	p<0.001
Clinical Characteristics			
Atrial Fibrillation or Flutter at Screening	717 (31.8%)	1528 (25.6%)	p<0.001
Hypertension History	1573 (69.7%)	4211 (70.5%)	p=0.46
Type 2 diabetes mellitus	954 (42.2%)	2355 (39.4%)	p=0.020
History of stroke	240 (10.6%)	514 (8.6 %)	p=0.004
Ischemic heart failure etiology	1213 (53.7%)	3202 (53.6%)	p=0.92
History of Myocardial Infarction	960 (42.5%)	2475 (41.4%)	p=0.37
LVEF - %	23.4 ± 5.2	27.8 ± 6.2	p<0.001
NYHA Classification			p<0.001
Class II	0 (0.0 %)	4368 (73.1%)	
Class III	2085 (92.3%)	1531 (25.6%)	
Class IV	173 (7.7 %)	75 (1.3 %)	
KCCQ Total Symptom Score	56.2 [36.5, 77.1]	74.0 [54.2, 90.6]	p<0.001
Outpatient	63.5 [44.8, 83.3]	77.1 [58.3, 91.7]	p<0.001
Inpatient	47.4 [29.2,66.7]	57.3 [37.5,76.0]	p<0.001
SBP — mmHg	113.8 ± 15.0	117.5 ± 15.4	p<0.001
Heart rate — beats/min	74.3 ± 12.5	71.7 ± 11.9	p<0.001
NT-proBNP — pg/mL	2804 [1450, 5795]	1768 [878 ,3521]	p<0.001
Cardiac Troponin I — ng/L	34 [19, 64]	24 [12, 47]	p<0.001
eGFR — mL/min/1.73m2	55.1 [41.8, 69.9]	60.0 [45.4, 75.5]	p<0.001

Heart Failure Therapies			
ACEi, ARB or ARNi	1873 (82.9%)	5286 (88.5%)	p<0.001
ARNi	447 (19.8%)	1154 (19.3%)	p=0.62
BB	2093 (92.7%)	5670 (94.9%)	p<0.001
MRA	1768 (78.3%)	4629 (77.5%)	p=0.43
SGLT2 Inhibitors	50 (2.2 %)	168 (2.8 %)	p=0.13
Ivabradine	188 (8.3 %)	345 (5.8 %)	p<0.001
Digitalis glycosides	436 (19.3%)	949 (15.9%)	p<0.001
Cardiac Resynchronization Therapy	372 (16.5%)	786 (13.2%)	p<0.001
Implantable Cardioverter Defibrillator	807 (35.7%)	1807 (30.2%)	p<0.001

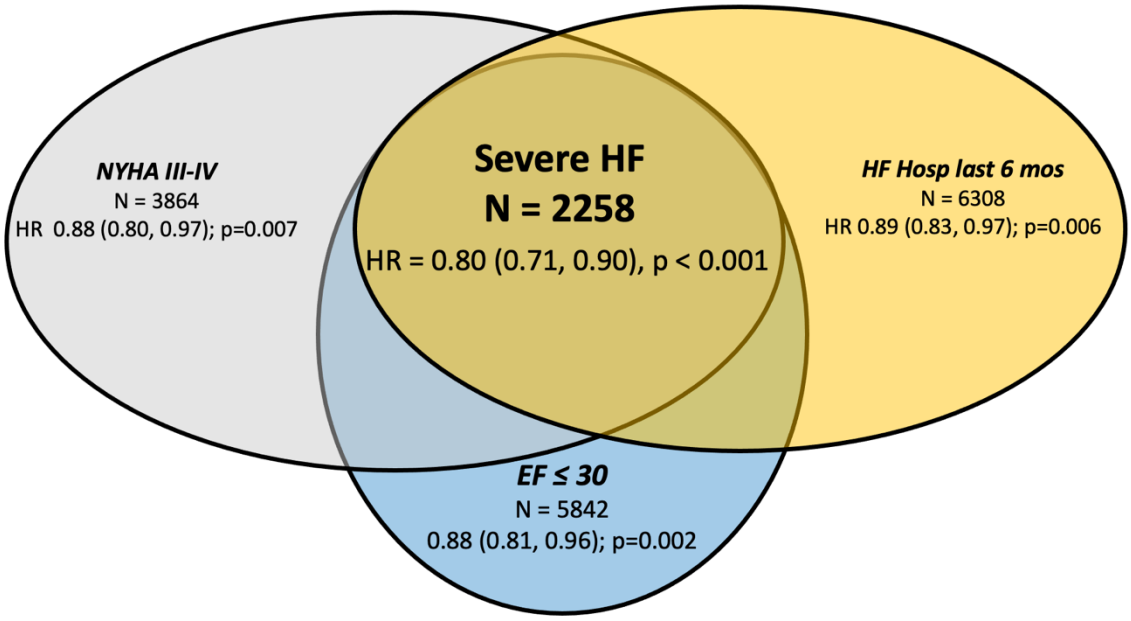
LVEF = left ventricular ejection fraction, NYHA = New York Heart Association, KCCQ = Kansas City Cardiomyopathy Questionnaire, SBP = systolic blood pressure, NT-proBNP = amino-terminal-b-type natriuretic peptide, eGFR = estimated glomerular filtration rate, ACEi = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, ARNi = angiotensin receptor neprilysin inhibitor, BB = beta blocker, MRA = mineralocorticoid receptor antagonists, SGLT2 = sodium glucose co-transport-2

eTable 2. Tolerability by Treatment Group and Severe Heart Failure Status

Variable	Week 0		Week 24			
	OM	Placebo	OM	Placebo	Ratio or Difference	p-value
Severe HF						
Systolic BP (mm Hg) week 0 to 24 (n = 1849)	114.0±15.3	113.5±14.7	116.7±17.3	116.0±17.7	0.6 (-0.7, 2.0)	p=0.35
Heart rate (beats/min) week 0 to 24 (n = 1850)	74.5±12.7	74.1±12.3	71.2±12.3	73.0±12.8	-1.9 (-2.9, -0.8)	p<0.001
Potassium (mmol/L) week 0 to 24 (n = 1761)	4.53±0.57	4.56±0.56	4.52±0.57	4.56±0.58	-0.03 (-0.08, 0.02)	p=0.27
Creatinine (mg/dl) week 0 to 24 (n = 1787)	1.39±0.50	1.36±0.48	1.37±0.55	1.38±0.56	-0.01 (-0.04, 0.02)	p=0.53
NT-proBNP (pg/ml) week 0 to 24 [Ratio] (n = 1773)	2758 [1480, 5838]	2834 [1416, 5732]	1837 [856, 4043]	2030 [918, 4703]	0.86 (0.78, 0.95)	p=0.002
Troponin I (ng/L) week 0 to 24 [Median Difference] (n = 1613)	34 [19, 63]	34 [19, 64]	41 [18, 74]	30 [14, 60]	5 (3, 7)	p<0.001
Troponin I (ng/L) week 0 to 24 [Ratio] (n = 1613)	34 [19, 63]	34 [19, 64]	41 [18, 74]	30 [14, 60]	1.27 (1.19, 1.37)	p<0.001
Not Severe HF						
Systolic BP (mm Hg) week 0 to 24 (n = 5383)	117.1±15.4	117.9±15.4	118.4±16.8	119.6±17.9	-0.7 (-1.5, 0.1)	p=0.07
Heart rate (beats/min) week 0 to 24 (n = 5383)	71.7±12.0	71.6±11.9	69.6±11.3	71.0±11.6	-1.4 (-2.0, -0.9)	p<0.001
Potassium (mmol/L) week 0 to 24 (n = 5251)	4.57±0.51	4.57±0.51	4.56±0.51	4.55±0.52	0.01 (-0.02, 0.03)	p=0.58
Creatinine (mg/dl) week 0 to 24 (n = 5278)	1.27±0.45	1.28±0.45	1.29±0.49	1.28±0.48	0.01 (-0.00, 0.03)	p=0.14
NT-proBNP (pg/ml) week 0 to 24 [Ratio] (n = 5261)	1753 [864, 3479]	1795 [893, 3540]	1274 [531, 2731]	1391 [613, 2987]	0.91 (0.86, 0.95)	p<0.001

Troponin I (ng/L) week 0 to 24 [Median Difference] (n = 4758)	24 [12, 47]	24 [12, 46]	31 [13, 63]	22 [10, 45]	4 (3, 5)	p<0.001
Troponin I (ng/L) week 0 to 24 [Ratio] (n = 4758)	25 [11, 47]	25 [11, 47]	31 [13, 63]	22 [10, 45]	1.24 (1.20, 1.29)	p<0.001
BP = blood pressure, NT-proBNP = amino-terminal-b-type natriuretic peptide						

eFigure. Venn Diagram of Groups Defined by Specific Severe Heart Failure Criteria



HR = hazard ratio for treatment with omecamtiv mecarbil vs placebo for the primary endpoint of time to first heart failure event or cardiovascular death.