Supplemental Table 1: Echocardiogram and Endpoint Results in Subjects with LV Ejection Fraction <50% During the Treatment Period

Subject	Treatment Group	Visit/LVEF	NT-proBNP (ng/L)	Baseline Echo	W30 Echo	Endpoints Change (Baseline - W30)
1	Mava	D1/92% W6/35%* W30/83%	D1 - 220 W6 - 86 W30 -59	LVOT R/V: 96.4/104.4 mmHg E/e' sep: 16.4 E/e' lat: 23.9 LAVI: 30.0 mL/m^2	LVOT R/V: 8.2/10.5 mmHg E/e' sep: 10.1 E/e' lat: 7.9 LAVI: 22.4 mL/m^2	pVO2 -3.3 ml/kg/min NYHA II to I KCCQ +7.3
2	Mava	D1/70% W18/45% W30/65%	D1 - 416 W18 - 152 W30 - 203	LVOT R/V: 25.6/46.8 mmHg E/e' sep: 17.2 E/e' lat: 16.2 LAVI: 52.9 mL/m^2	LVOT R/V: 7.7/16.3 mmHg E/e' sep: 17.4 E/e' lat: 13.3 LAVI: 46.6 mL/m^2	pVO2 +6.6 ml/kg/min NYHA II to I KCCQ +21.9
3	Mava	D1/84% W18/43% W30/73%	D1 - 1342 W18 - 70 W30 - 166	LVOT R/V: 101.6/129.1 mmHg E/e' sep: 25.3 E/e' lat: missing LAVI: 50.0 mL/m^2	LVOT R/V: 41.7/53.9 mmHg E/e' sep: 16.1 E/e' lat: 11 LAVI: 26.3 mL/m^2	pVO2 +2.3 ml/kg/min NYHA III to II KCCQ -3.7
4	Mava	D1/70% W30/48% W38/73%	D1 - 434 W30 - 11 W38 - 163	LVOT R/V: 83.5/124.5 mmHg E/e' sep: 16.5 E/e' lat: 13.4 LAVI: 51.8 mL/m^2	LVOT R/V: 8.3/9.2 mmHg E/e' sep: 15.7 E/e' lat: 9.6 LAVI: 41.5 mL/m^2	pVO2 -2.1 ml/kg/min NYHA II to II KCCQ -2.1
5	Mava	D1/74% W30/49% W38/72%	D1 - 864 W30 - 121 W38 - 1456	LVOT R/V: 11.6/69.2 mmHg E/e' sep: 15.3 E/e' lat: 15.4 LAVI: 37.3 mL/m^2	LVOT R/V: 5.3/8.6 mmHg E/e' sep: 14.7 E/e' lat: 10 LAVI: 28.6 mL/m^2	pVO2 -3.1 ml/kg/min NYHA II to II KCCQ +21.4
6	Mava	D1/66% W30/49% W38/70%	D1 - 634 W30 - 1164 W38 - 830	LVOT R/V: 37.7/55.4 mmHg E/e' sep: 23.6 E/e' lat: 16 LAVI: 33.1 mL/m^2	LVOT R/V: 6.7/7.5 mmHg E/e' sep: 23.9 E/e' lat: 11.3 LAVI: 40.8 mL/m^2	pVO2 -0.3 ml/kg/min NYHA II to II KCCQ – no baseline
7	Mava	D1/80% W30/49% W38/50%	D1 - 136 W30 - 1494 W38 - ND	LVOT R/V: 71.2/83.9 mmHg E/e' sep: 14.8 E/e' lat: 8.3 LAVI: 45.5 mL/m^2	LVOT R/V: 16.8/15.5 mmHg E/e' sep: 24.6 E/e' lat: 15 LAVI: 38.1 mL/m^2	pVO2 -8.8 ml/kg/min NYHA III to II KCCQ +34.9
8	Placebo	D1/54% W4/49% W30/60%	D1 - 434 W4 - 572 W30 - 681	LVOT R/V: 16.3/47.9 mmHg E/e' sep: 12.3 E/e' lat: 5.8 LAVI: 76.0 mL/m^2	LVOT R/V: 41.0/49.8 mmHg E/e' sep: 11.7 E/e' lat: 5.4 LAVI: 84.4 mL/m^2	pVO2 +0.7 ml/kg/min NYHA III to II KCCQ – no baseline
9	Placebo	D1/64% W12/42% W30/57%	D1 – 4858 W12 - 4345 W30 - 5252	LVOT R/V: 129.5/143.0 mmHg E/e' sep: 32.9 E/e' lat: 19.2 LAVI: 61.0 mL/m^2	LVOT R/V: 94.5/123.7 mmHg E/e' sep: 36.8 E/e' lat: 33.5 LAVI: 49.4 mL/m^2	pVO2 +0.1 ml/kg/min NYHA II to II KCCQ +21.3

D=Day, W=Week, LVEF=Left Ventricular Ejection Fraction, LVOT R/V=Left Ventricular Outflow Tract Gradient Rest/Valsalva, E/e' sep=E/e' septal, E/e' lat=E/e' lateral, LAVI=Left Atrial Volume Index,
pVO2=peak oxygen consumption, NYHA=New York Heart Association, KCCQ=Kansas City Cardiomyopathy Questionnaire

[*]Subject 1 with SAE of stress cardiomyopathy at W6. Recovered and resumed dosing after 8-week interruption.

Supplemental Table 2: Echocardiogram, NYHA, and Biomarker Results in Subjects who Discontinued Treatment

Subject	Treatment Group	Reason for Treatment Discontinuation	Baseline Values	Nearest Available Measure to Treatment discontinuation*	Last Available Measure after Treatment Discontinuation
1	Mava	Atrial Fibrillation	NYHA: III NT-proBNP: 4173 ng/L LVEF: 63% LVOT R/V: 57.5/64.6 mmHg E/e' sep: 27.1 E/e' lat: 25.4 LAVI: 51.9 mL/m^2	**W18**† NYHA: I NT-proBNP: 617 ng/L LVEF: 59% LVOT R/V: 11.2/16.8 mmHg E/e' sep: 20.7 E/e' lat: 10 LAVI: 49.7 mL/m^2	**W30** NYHA: II NT-proBNP: 4128 ng/L LVEF: 68% LVOT R/V: 28.7/47.3 mmHg E/e' sep: 30.6 E/e' lat: 28.1 LAVI: 51.2 mL/m^2
2	Mava	Syncope	NYHA: II NT-proBNP: 199 ng/L LVEF: 77% LVOT R/V: 23.4/63.4 mmHg E/e' sep: 17.1 E/e' lat: 15.5 LAVI: 34.9 mL/m^2	**W12** NYHA: II NT-proBNP: 22 ng/L LVEF: 70% LVOT R/V: 22.3/25.8 mmHg E/e' sep: 7.1 E/e' lat: NA LAVI: NA	**ET**‡ NYHA: II NT-proBNP: 73 ng/L LVEF: 66% LVOT R/V: 21.9/104.9 mmHg E/e' sep: 13.5 E/e' lat: 9.4 LAVI: 34.3 mL/m^2
3	Mava	Withdrew for Personal reason	NYHA: II NT-proBNP: 1231 ng/L LVEF: 80% LVOT R/V: 51.8/53.3 mmHg E/e' sep: 15.8 E/e' lat: 11 LAVI: 57.1 mL/m^2	**W4**§ NYHA: III NT-proBNP: 1040 ng/L LVEF: 74% LVOT R/V: 65.3/74.7 mmHg E/e' sep: 14.4 E/e' lat: NA LAVI: NA	**W6** NYHA: III NT-proBNP: 1024 ng/L LVEF: 69% LVOT R/V: 37.7/55.4 mmHg E/e' sep: 12.5 E/e' lat: NA LAVI: NA
4	Mava	Schedule conflict at Wk 30 (no CPET performed)	NYHA: II NT-proBNP: 1781 ng/L LVEF: 71% LVOT R/V: 87.2/89.5 mmHg E/e' sep: 12.4 E/e' lat: 9 LAVI: 47.5 mL/m^2	**W30** NYHA: I NT-proBNP: 364 ng/L LVEF: 76% LVOT R/V: 8.5/24.4 mmHg E/e' sep: 6.8 E/e' lat: 5.9 LAVI: 38 mL/m^2	**W38** NYHA: II NT-proBNP: 1423 ng/L LVEF: 76% LVOT R/V: 64.6/81.7 mmHg E/e' sep: 12.3 E/e' lat: 7.9 LAVI: 41.5 mL/m^2
5	Placebo	Sudden death	NYHA: III NT-proBNP: 88 ng/L LVEF: 67% LVOT R/V: 12.1/24.6 mmHg E/e' sep: 14.7 E/e' lat: 11.5 LAVI: 25.3 mL/m^2	**W22** NYHA: II NT-proBNP: 239 ng/L LVEF: 77% LVOT R/V: 19.5/83.2 mmHg E/e' sep: 16.1 E/e' lat: 14.8 (W18) LAVI: 29.8 mL/m^2	NA

				(W18)	
6	Placebo	Withdrew for personal reason	NYHA: II NT-proBNP: 227 ng/L LVEF: 69% LVOT R/V: 18.3/23.2 mmHg E/e' sep: 11.2 E/e' lat: 8.9 LAVI: 31.7 mL/m^2	W**4** NYHA: II NT-proBNP: 404 ng/L LVEF: 69% LVOT R/V: 38.7/42.3 mmHg E/e' sep: 11 E/e' lat: 7.4 LAVI: 38 mL/m^2	**ET**[‖] NYHA: II NT-proBNP: 454 ng/L LVEF: 71% LVOT R/V: 33.6/46.8 mmHg E/e' sep: 9.4 E/e' lat: 6.7 LAVI: 31.8 mL/m2
7	Placebo	No W30 assessments due to COVID19 restrictions for visit	NYHA: II NT-proBNP: 1837 ng/L LVEF: 74% LVOT R/V: 88/104.9 mmHg E/e' sep: 27.4 E/e' lat: NA LAVI: 36.1 mL/m^2	**W26** NYHA: II NT-proBNP: 2360 ng/L (W22) LVEF: 75% LVOT R/V: 87.2/94.9 mmHg E/e' sep: 34.2 E/e' lat: 19.4 (W18) LAVI: 43.2 mL/m^2 (W18)	NA

NYHA = New York Heart Association, W=Week, ET=early termination visit, LVEF=Left Ventricular Ejection Fraction, LVOT R/V=Left Ventricular Outflow Tract gradient Rest/Valsalva, E/e' sep=E/e' septal, E/e' lat=E/e' lateral,
LAVI=Left Atrial Volume Index, NA=Not available

[*]Values are shown for nearest visit *prior to* study drug discontinuation unless otherwise noted

[†]Echocardiogram values were obtained at a visit 12 days *after* study drug discontinuation.

[‡]ET visit occurred 8 days after W12 visit.

[§]W4 values were obtained 20 days *after* study drug discontinuation; subject on study drug only 10 days.

[‖]ET visit occurred 1 day after study drug discontinuation

Supplemental Table 3: Changes from Baseline in Resting Echocardiographic Parameters by Complete Resolution of Mitral Valve SAM

		Mavacamten (N = 123)		**Placebo (N = 128)**
	n	**Change (95% CI) from baseline at week 30**	**n**	**Change (95% CI) from baseline at week 30**
LVOT resting gradient, mmHg				
SAM Complete Resolution	76	-45.6 (-52.4, -38.9)	32	-11.5 (-21.8, -1.3)
SAM Non-Resolution	18	-31.9 (-42.1, -21.7)	64	-5.1 (-12.2, 2.0)
LVOT Valsalva gradient, mmHg				
SAM Complete Resolution	76	-51.1 (-59.3, -42.8)	33	-20.1 (-30.8, -9.5)
SAM Non-Resolution	18	-44.2 (-61.0, -27.3)	64	-10.1 (-17.7, -2.5)
LAVI, mL/m2				
SAM Complete Resolution	75	-8.1 (-10.0, -6.2)	33	1.2 (-1.7, 4.0)
SAM Non-Resolution	17	-9.4 (-12.9, -6.0)	63	-1.5 (-3.8, 0.8)
E/E' Septal Ratio				
SAM Complete Resolution	72	-3.6 (-5.1, -2.1)	31	0.3 (-1.4, 2.0)
SAM Non-Resolution	17	-3.8 (-6.6, -1.0)	61	-0.4 (-1.5, 0.8)
E/E' Lateral Ratio				
SAM Complete Resolution	67	-3.9 (-5.2, -2.7)	28	-1.6 (-2.6, -0.6)
SAM Non-Resolution	17	-4.6 (-6.4, -2.7)	57	0.5 (-1.0, 1.9)

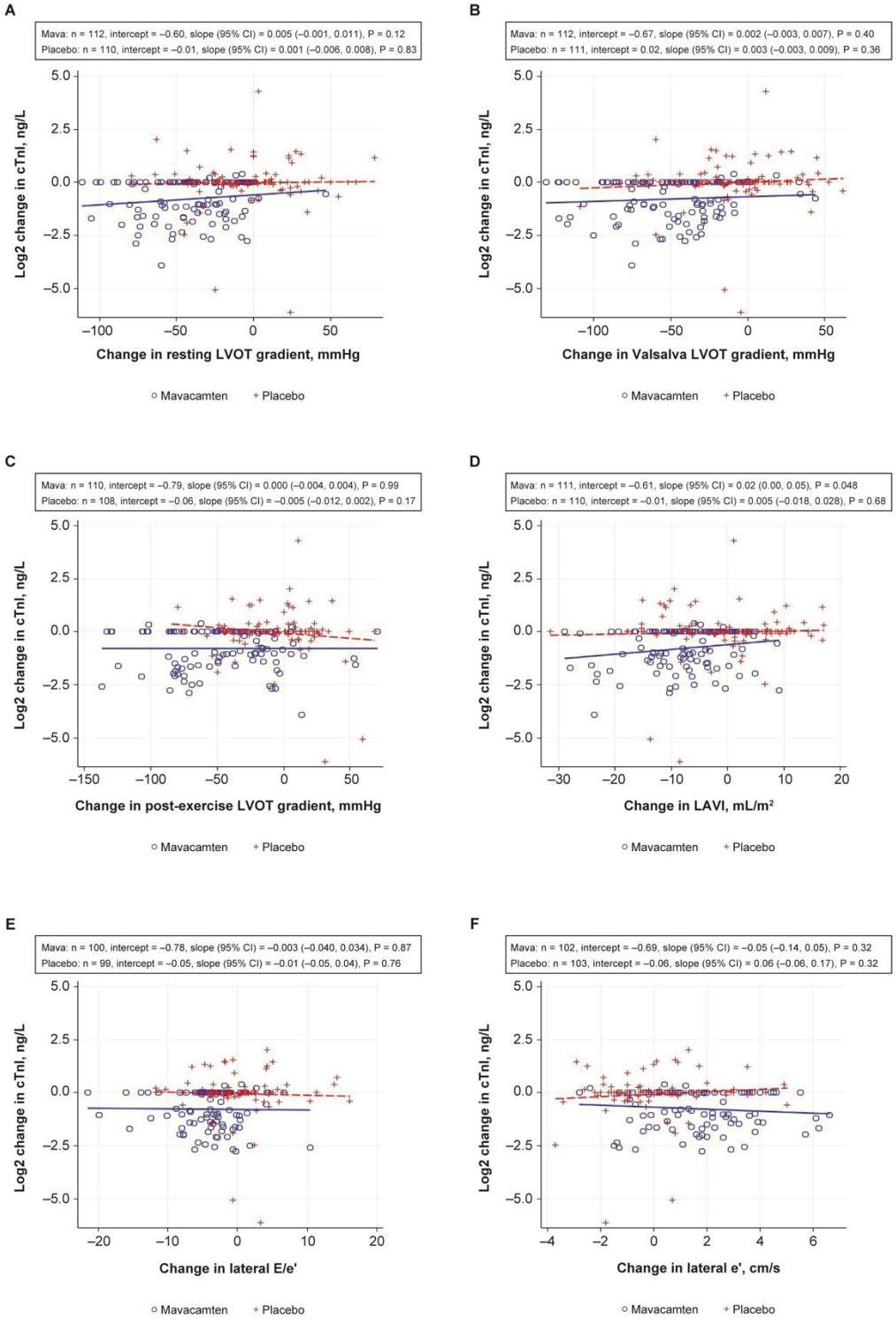
Values are mean (95% CI) unless otherwise indicated. CI = confidence interval; SAM = systolic anterior motion; LVOT = left ventricular outflow tract; LAVI = left atrial volume index; E/e' = ratio between early mitral inflow velocity and mitral annular early diastolic velocity.

Supplemental Table 4: **Linear Regression of Log2 Changes in NT-proBNP on Changes in Resting LVOT Gradient**

	Mavacamten (N = 123)				Placebo (N = 128)			
	n	**Intercept**	**Slope (95%CI)**	**p-value**	**n**	**Intercept**	**Slope (95%CI)**	**p-value**
Baseline Resting LVOT gradient, mmHg	114	−1.60	0.02 (0.01, 0.03)	<0.0001	120	0.03	−0.001 (−0.006, 0.003)	0.63
By Resting LVOT gradient < 50 or >= 50 mmHg								
Baseline LVOT Resting<50 mmHg	55	-1.30	0.04 (0.01, 0.07)	0.01	63	0.07	-0.002 (-0.01, 0.01)	0.61
Baseline LVOT Resting>=50 mmHg	59	-1.73	0.02 (0.00, 0.03)	0.02	57	-0.03	-0.002 (-0.01, 0.00)	0.55
By Resting LVOT gradient < 30 or >= 30 mmHg								
Baseline LVOT Resting<30 mmHg	32	-1.51	0.03 (-0.04,0.10)	0.36	37	0.03	0.001 (-0.01, 0.02)	0.84
Baseline LVOT Resting>=30 mmHg	82	-1.60	0.02 (0.01, 0.03)	<0.001	83	0.005	-0.002 (-0.01, 0.00)	0.47

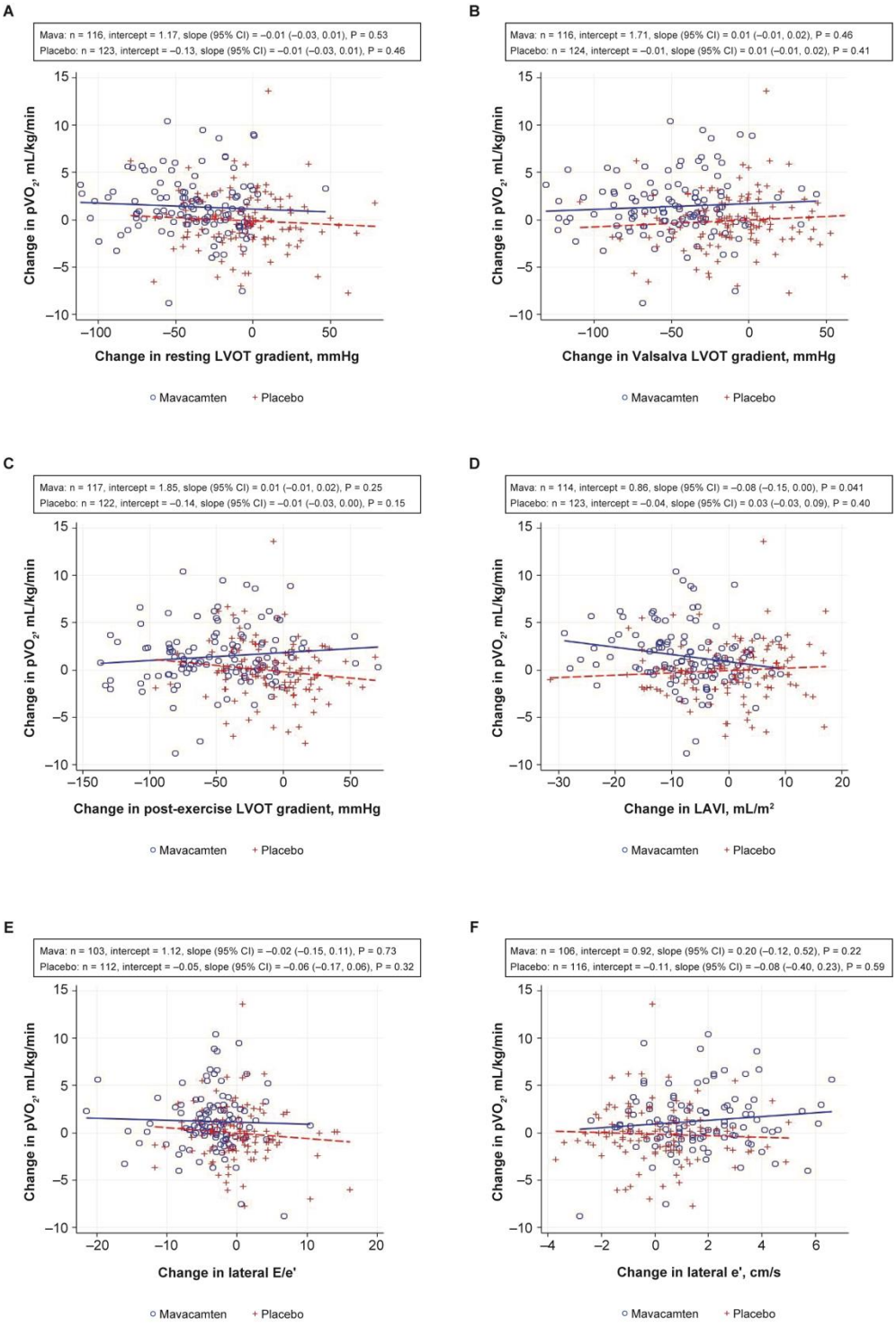
LVOT = left ventricular outflow tract; NT-proBNP = N-terminal pro B-type natriuretic peptide

Figure S1. Relationship of Log2 Change in cTnI on Changes in Echocardiographic Parameters



Scatter plots show the linear regression of the week 30 to baseline log2 change in cTnI on changes in resting LVOT gradient (A), Valsalva LVOT gradient (B), post-exercise LVOT gradient (C), LAVI (D), lateral E/e' (E), and lateral e' (F). Abbreviations as in Tables 1 and 2.

Figure S2. Relationship of Log2 Change in pVO2 on Changes in Echocardiographic Parameters



Scatter plots show the linear regression of the week 30 to baseline log2 change in pVO2 on changes in resting LVOT gradient (A), Valsalva LVOT gradient (B), post-exercise LVOT gradient (C), LAVI (D), lateral E/e' (E), and lateral e' (F). Abbreviations as in Tables 1 and 2.