SUPPLEMENTAL MATERIAL

Table S1. Mavacamten Dose by Visit (Safety Population).

	Mavacamten dose, mg/day				
Patient	**Baseline**	**Week 6**	**Week 156**	**Week 180**	**Week 204**
Patient 1	5	15	15	15*	ND
Patient 2	5	10	10	10	ND
Patient 3	5	5	5	5	ND
Patient 4	5	10	5	5	5
Patient 5	5	5[†]	–	–	–
Patient 6	5	5	5	5	ND
Patient 7	5	15	10	10	10
Patient 8[‡]	5	10	10	10	10
Patient 9	5	10	10	10	10
Patient 10	5	15	15	10**	10
Patient 11	5	5	5	5	ND
Patient 12	5	10	10	10	ND
Patient 13	5	10	10	10	ND

ND indicates no data available.

Patient numbers here are not related to patient numbers in Supplemental Tables 3 and 4.

*Dose at week 184.

[†]Patient discontinued treatment at week 26.

[‡] Patient had a dose increase by error from 10 mg to 15 mg at an unscheduled visit at week 74. The dose was subsequently decreased to 10 mg at week 75. This was noted as a protocol deviation.

**Dose at week 188.

Table S2. Exposure-Adjusted Incidence of TEAEs by ECI and SSs (Safety Population).

ECI/SS category Preferred term	Mavacamten (n=13)		
	Number of patients	Patient-years*	Exposure-adjusted incidence, per 100 patient-years
Patients with at least one ECI	12	18.4	65.15
Major adverse cardiovascular events	2	43.6	4.58
Subdural hematoma	1	46.8	2.14
Troponin increased	1	44.1	2.27
Atrial fibrillation	1	46.0	2.17
Syncope/presyncope [broad]	2	39.6	5.06
Dizziness	2	39.6	5.06
Orthostatic hypotension	1	44.9	2.23
Cardiac failure	1	46.7	2.14
Ejection fraction decreased	1	46.7	2.14
Orthostatic Hypotension	1	44.9	2.23
QTc prolongation	1	46.9	2.13
Hepatic events	2	46.8	4.27
Alanine aminotransferase increased	1	47.0	2.13
Aspartate aminotransferase increased	1	47.1	2.12
Dizziness (ECI)	4	32.9	12.16
Dizziness postural	3	38.7	7.74
Dizziness	2	39.6	5.06
Dizziness exertional	1	43.6	2.29
Accidents and injuries	3	38.3	7.84
Fall	2	41.4	4.83
Ligament sprain	1	43.7	2.29
Lumbar vertebral fracture	1	44.1	2.27
Spinal compression fracture	1	44.1	2.27
Accidents and injuries (SAEs)	1	44.1	2.27
Lumbar vertebral fracture	1	44.1	2.27
Spinal compression fracture	1	44.1	2.27

Gastrointestinal events	4	40.5	9.89
Diarrhea	2	44.1	4.54
Abdominal discomfort	1	44.8	2.23
Abdominal pain	1	43.9	2.28
Abdominal pain upper	1	47.1	2.12
Constipation	1	47.2	2.12
Nausea	1	44.9	2.23
Vomiting	1	44.9	2.23
Hypersensitivity	3	42.8	7.01
Dermatitis contact	2	43.2	4.63
Eczema	1	46.8	2.14
Eczema nummular	1	45.7	2.19
Ventricular tachycardia	1	44.2	2.26

ECI indicates event of clinical interest; QTc, corrected QT interval; SAE, serious adverse event; SS, special situation; TEAE, treatment-emergent adverse event.

*For exposure-adjusted incidence rates, the exposure time to first event was calculated as total duration of exposure up to the first occurrence of the event. For participants with no event, the time was censored at the last follow-up time within the treatment-emergent period. For participants with multiple events, the time to first event was considered.

Table S3. Selected individual data at baseline, week 12 and week 16 for the parent study PIONEER-HCM and at baseline for the extension study PIONEER-OLE.

Patient	NT-proBNP, ng/L				Valsalva LVOT gradient, mm Hg				LVEF, resting, %			
	PIONEER-HCM			PIONEER-OLE	PIONEER-HCM			PIONEER-OLE	PIONEER-HCM			PIONEER-OLE
	Baseline	Week 12	Week 16	Baseline	Baseline	Week 12	Week 16	Baseline	Baseline	Week 12	Week 16	Baseline
1	90	22	248	176	111	22	70	77	74	70	75	76
2	679	170	990	745	70	41	38	98	73	75	ND	77
3	835	198	1307	1382	54	18	81	67	76	65	65	73
4	660	27	65	545	176	5	20	ND	65	51	67	65
5	1551	233	152	559	118	5	10	91	67	52	61	66
6	183	1018	739	172	65	7	8	32	70	50	64	65
7	91	50	331	384	108	19	103	67	69	63	67	67
8	9680	1199	4734	3908	159	124	196	156	72	73	77	77
9	5796	2516	8678	7736	97	89	93	114	73	73	73	69
10	4165	2905	5133	5135	ND	76	141	107	70	77	74	79

11	789	41	69	351	109	6	10	103	77	50	68	74
12	36	20	40	42	60	26	31	94	76	68	ND	76
13	457	494	467	704	103	41	16	72	75	74	80	72

LVEF indicates left ventricular ejection fraction; LVOT, left ventricular outflow tract; ND, no data available; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Patient numbers here are not related to patient numbers in Supplemental Tables 1 and 4.

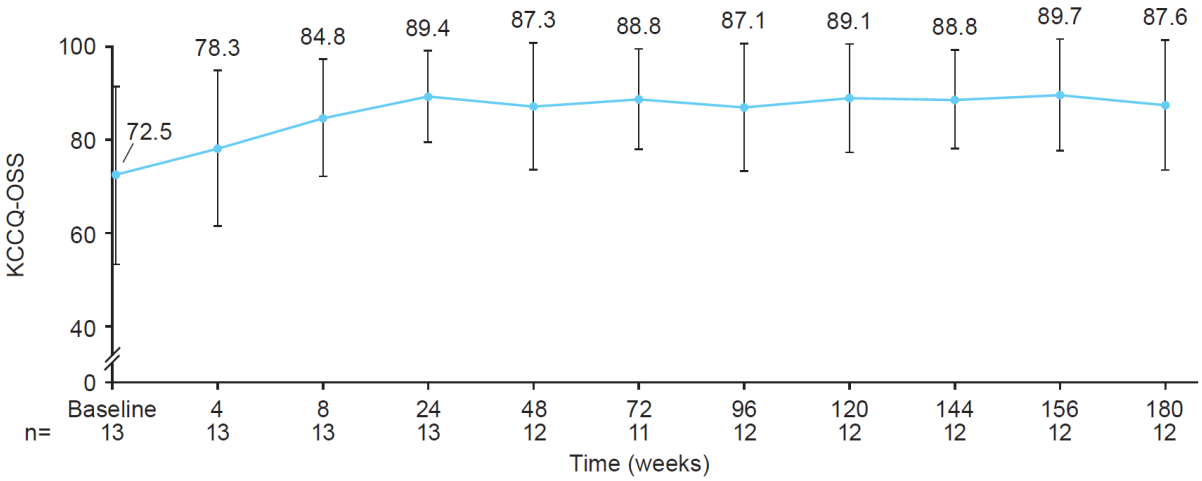
Table S4. Individual Resting LVOT Gradients ≥30 mm Hg and Valsalva Gradients ≥50 mm Hg at Week 180, and Post-exercise LVOT Gradients ≥50 mm Hg at Week 156 (Safety Population).

Week 180		**Week 156**
Resting LVOT gradient ≥30 mm Hg (n=3)	**Valsalva LVOT gradient ≥50 mm Hg (n=1)**	**Post-exercise LVOT gradient ≥50 mm Hg (n=2)**
65 (Patient 1)	72 (Patient 1)	80 (Patient 1)
34 (Patient 2)		72 (Patient 2)
40 (Patient 3)		

LVOT indicates left ventricular outflow tract.

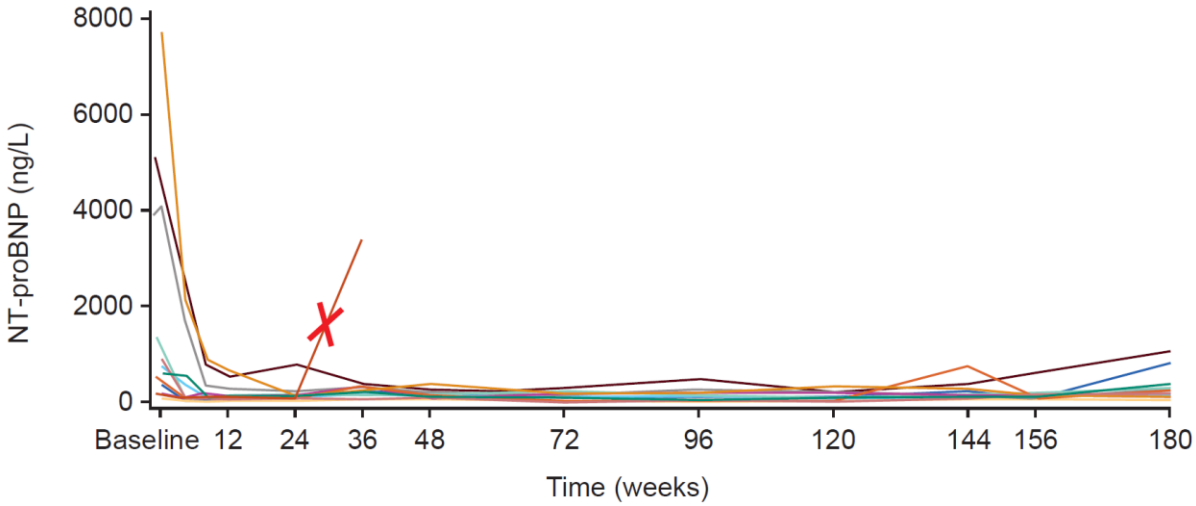
Data shown were read by the central cardiac laboratory and are presented as LVOT gradient in mm Hg (patient). Patient numbers here are not related to patient numbers in Supplemental Tables 1 and 3.

Figure S1. Mean (SD) KCCQ-OSS by visit.



KCCQ-OSS indicates Kansas City Cardiomyopathy Questionnaire-Overall Summary Score; SD, standard deviation.

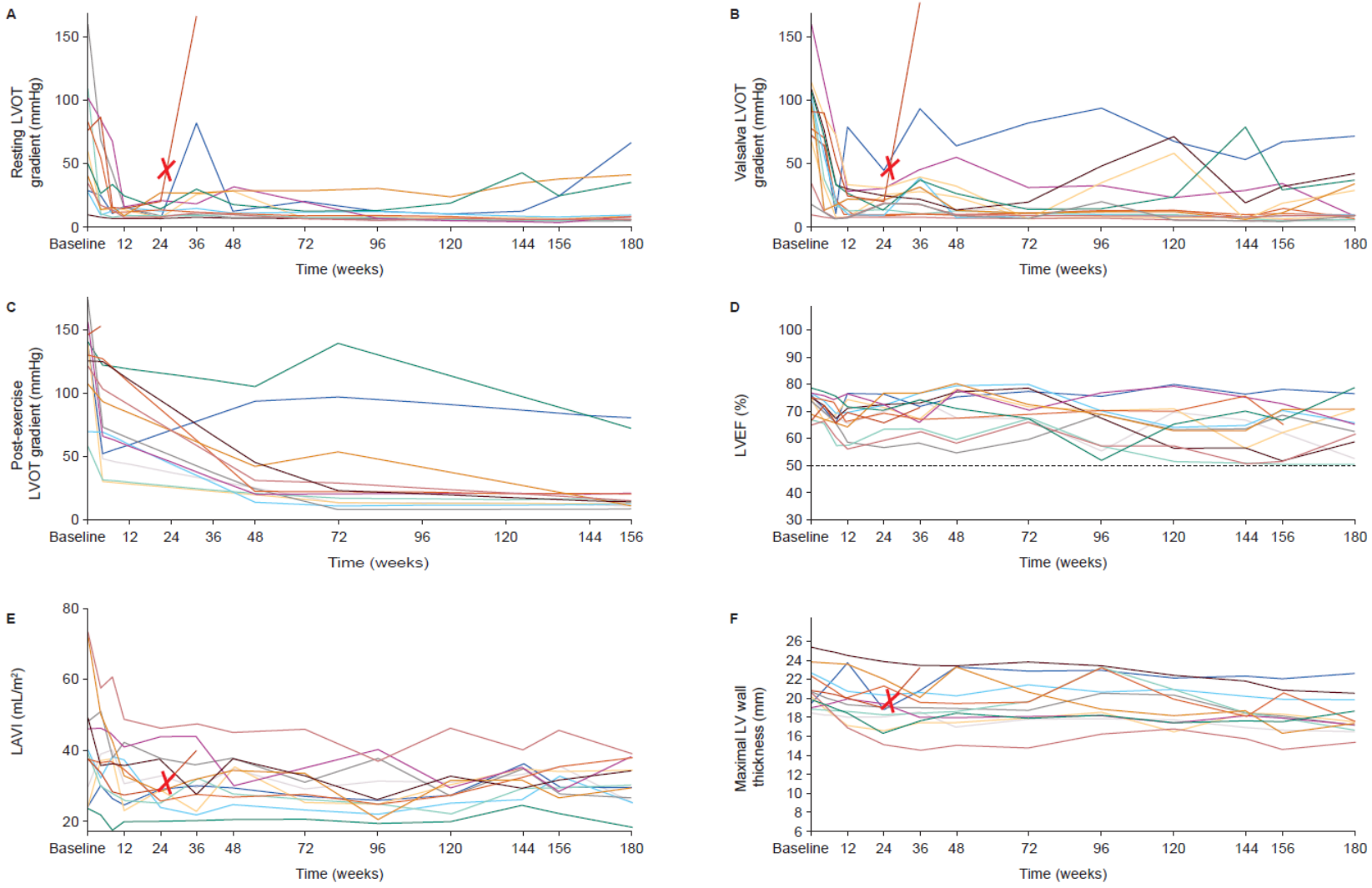
Figure S2. Individual serum NT-proBNP levels by visit.



The patient with an elevated value at Week 36 discontinued study treatment at week 26 owing to a serious adverse event unrelated to the study drug (cholangiocarcinoma). The two patients with elevated values at Week 180 were off treatment at the time of the visit (one due to subdural hematoma and one due to LVEF<50%). They both resumed treatment subsequently.

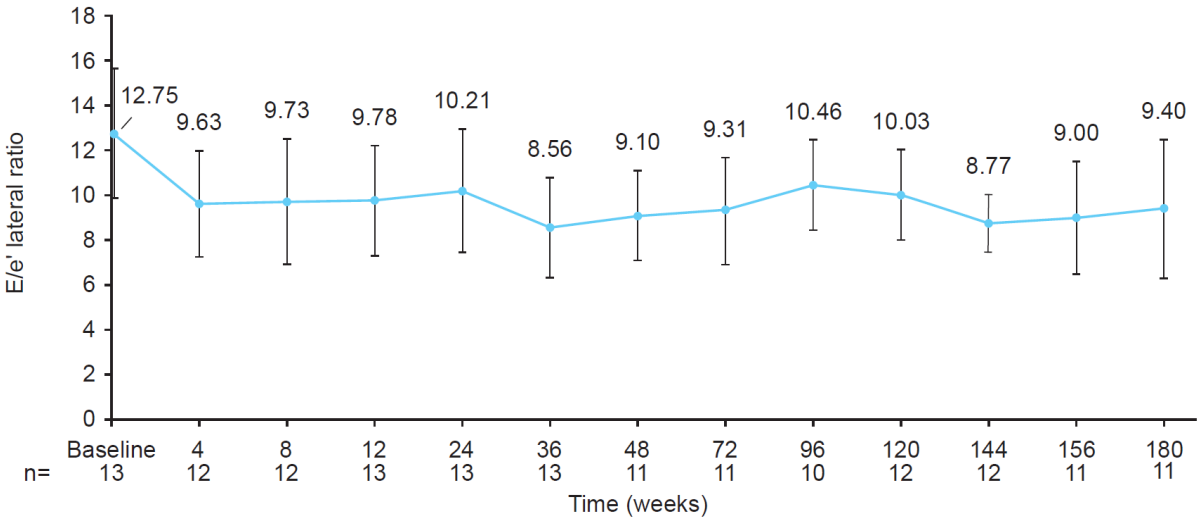
NT-proBNP indicates N-terminal pro-B-type natriuretic peptide.

Figure S3. Individual echocardiographic outcomes by visit.



A, Resting LVOT gradient. **B,** Valsalva LVOT gradient. **C,** Post-exercise LVOT gradient. **D,** LVEF. **E,** LAVI. **F,** Maximal left ventricular wall thickness. Dashed line on part D indicates a left ventricular ejection fraction of 50% (considered to be the threshold for left ventricular systolic dysfunction). The patient with elevated LVOT gradients at Week 36 discontinued study treatment at week 26 owing to a serious adverse event unrelated to the study drug (cholangiocarcinoma). Two patients were off treatment at the time of the Week 180 visit (one due to subdural hematoma and one due to LVEF<50%). They both resumed treatment subsequently. LAVI indicates left atrial volume index; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro-B-type natriuretic peptide; QTc, corrected QT interval.

Figure S4. Mean (SD) E/e' lateral ratio by visit.



E/e' indicates the ratio between early mitral inflow velocity and mitral annular early diastolic velocity; SD, standard deviation.