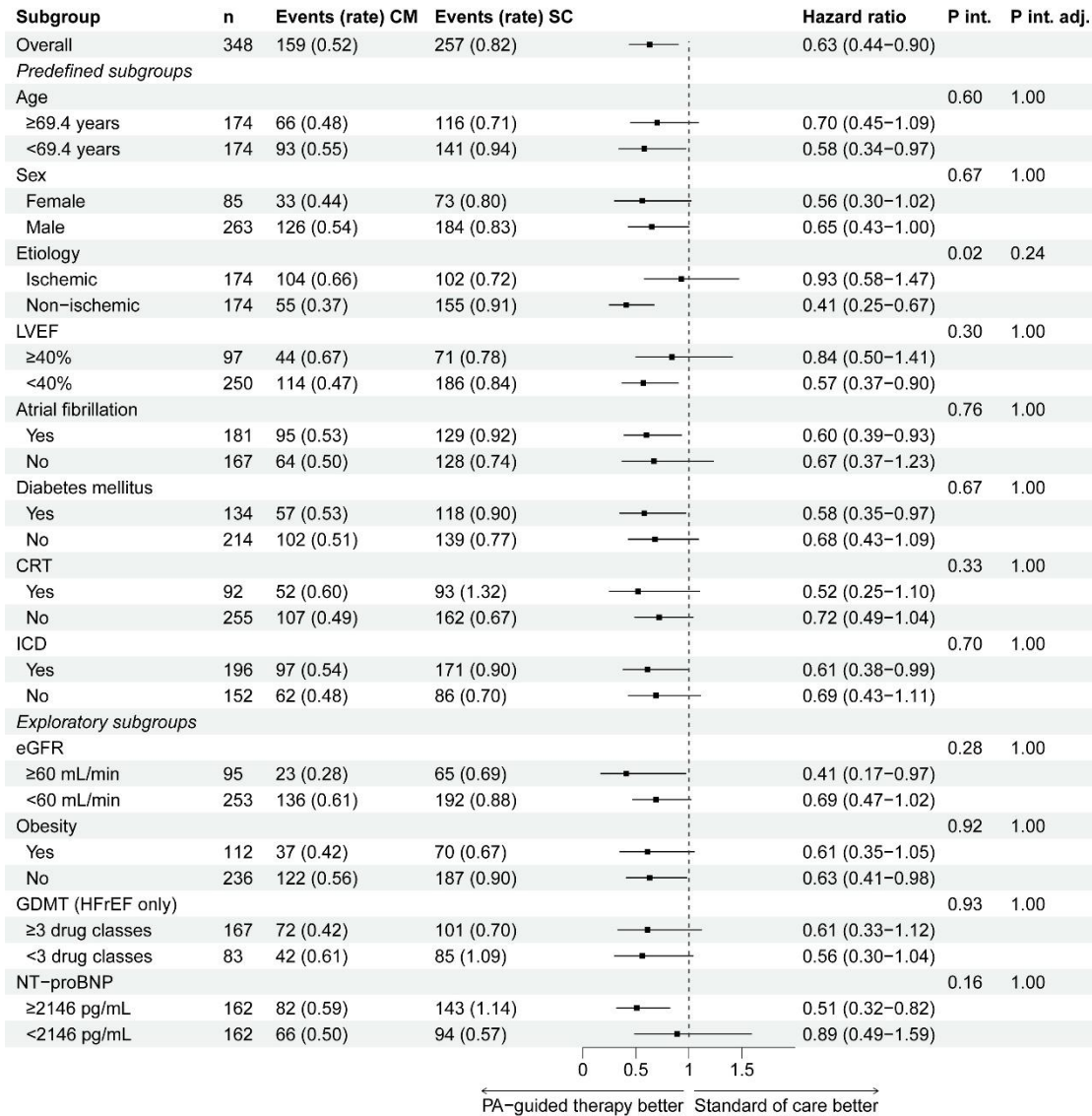


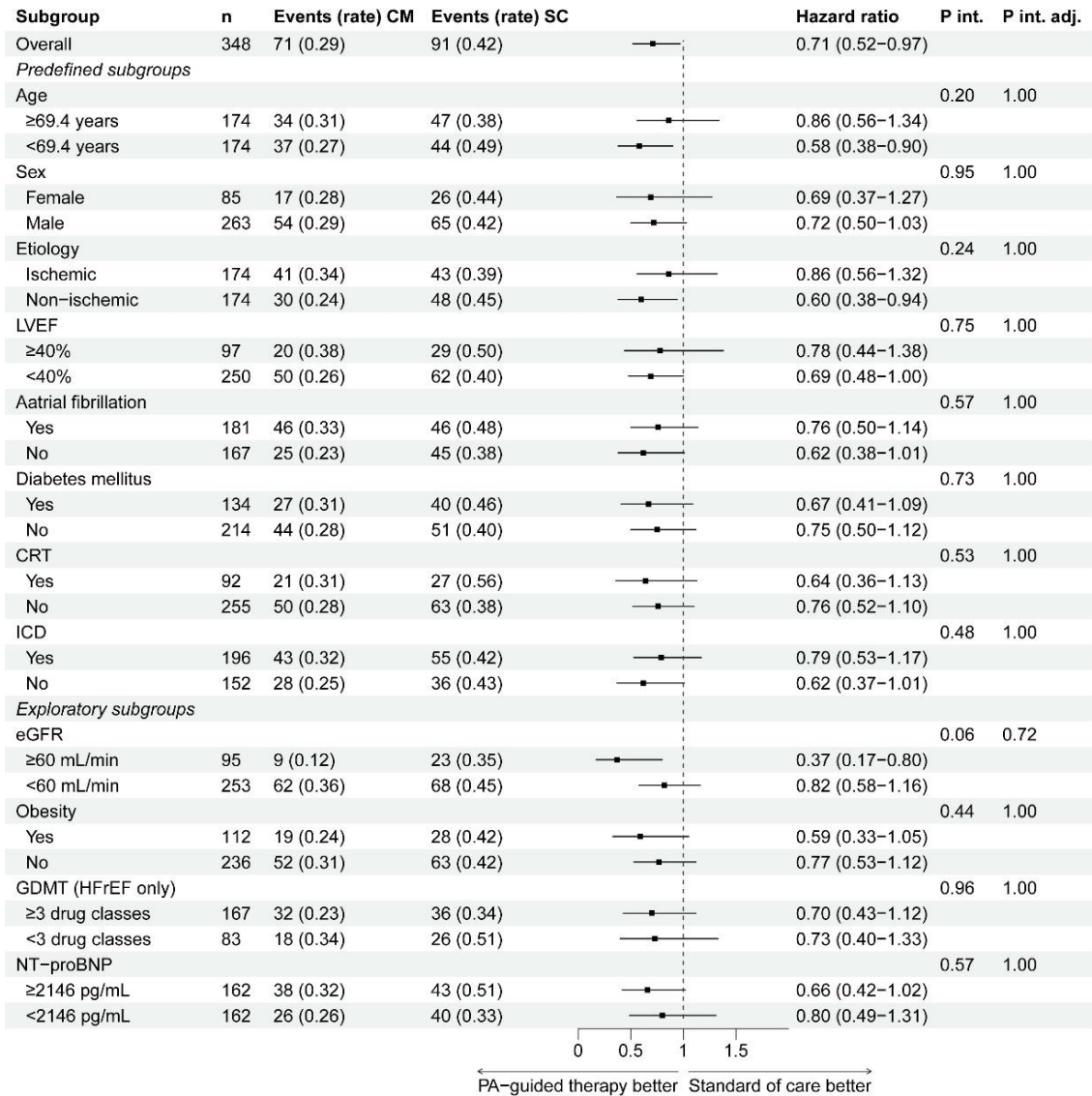
Supplementary material

Figure S1. Total heart failure hospitalizations and all-cause mortality.



Rate: events/patient-year; CM: CardiMEMS (PA-guided therapy) group; SC: standard of care group; P int: P interaction; P int adj: Pinteraction adjusted; LVEF: left ventricular ejection fraction; CRT: cardiac resynchronization therapy; ICD: implantable cardiac defibrillator; eGFR: estimated glomerular filtration rate; GDMT: guideline-directed medical therapy; HFrEF: heart failure with a reduced ejection fraction.

Figure S2. Time to first heart failure hospitalization or cardiovascular mortality.



Rate: events/patient-year; CM: CardiMEMS (PA-guided therapy) group; SC: standard of care group; P int: P interaction; P int adj: Pinteraction adjusted; LVEF: left ventricular ejection fraction; CRT: cardiac resynchronization therapy; ICD: implantable cardiac defibrillator; eGFR: estimated glomerular filtration rate; GDMT: guideline-directed medical therapy; HFrEF: heart failure with a reduced ejection fraction.

Table S1. Full in- and exclusion criteria of MONITOR-HF.

| Inclusion criteria | Exclusion criteria |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Written informed consent obtained from subject aged ≥ 18 years. | 1. Subjects with an active infection |
| 2. Diagnosis of chronic HF* (≥ 3 months) in NYHA functional Class III with at least 1 HF hospitalization** or urgent visit with the necessity of intravenous (IV) diuretic therapy within 12 months of baseline visit (independent of EF %***). | 2. Subjects with history of recurrent (>1) pulmonary embolism or deep vein thrombosis |
| 3. Subjects with reduced EF (HFrEF) should be treated according to National and International (ESC) guidelines* for optimal or maximum tolerated doses of GDMT HF medication and evaluated for ICD or CRT therapy, if indicated. | 3. Subjects who have had a major cardiovascular event (e.g., myocardial infarction, open heart surgery, stroke) within 2 months. |
| 4. Subjects with a BMI ≤ 35 kg/m ² . Subjects with BMI >35 kg/m ² will require their chest circumference to be measured at the axillary level | 4. Subjects with Cardiac Resynchronization Therapy device (CRT) implanted |
| 5. Subjects willing and able to comply with the follow-up requirements of the study and able to comply with the daily readings. | 5. Subjects with a Glomerular Filtration Rate (GFR) |
| | 6. Subjects with complex congenital heart disease or mechanical right heart valve(s) |
| | 7. Subjects with known pulmonary arterial hypertension (WHO category 1 or 4/5) were PA pressure are most likely not responsive to cardiac treatment. |
| | 8. Subjects scheduled for or likely to undergo heart-transplantation or VAD within 6 months of baseline visit. |
| | 9. Subjects with known coagulation disorders or allergy to aspirin, and/or clopidogrel |

*according the ESC guidelines for heart failure 2016 definition for heart failure or subsequent versions of the ESC guidelines for heart failure 2021 during the course of the study and/or subsequent updates of recommendations in treatment of heart failure. **defined as an unscheduled HF admission longer than 6 hours and/or use of i.v. diuretics. ***patients diagnosed with heart failure according to ESC guideline definitions with either HFrEF, HFmrEF and HFpEF are eligible for participation in the study. In line with GCP, a patient cannot participate in any other intervention study (WMO-plichtig onderzoek). Additionally, a patient cannot participate in any other intervention study or other active telemonitoring programme (on HF parameters) during the study.

NYHA: New York Heart Association; HF: heart failure; EF: ejection fraction; ESC: European Society of Cardiology; ICD: implantable cardioverter-defibrillator; CRT: cardiac resynchronization therapy; BMI: body mass index; GFR: glomerular filtration rate; PA: pulmonary artery.

Table S2. Baseline characteristics of MONITOR-HF (n=348, intention-to-treat population).

| | PA-guided therapy (n=176) | Standard of Care (n=172) |
|--------------------------------------------------------|---------------------------|--------------------------|
| Age | 69 (61-75) | 70 (61-75) |
| Sex | | |
| Male | 138 (78.4%) | 125 (72.7%) |
| Female | 38 (78.4%) | 47 (27.3%) |
| BMI, kg/m ² | 27.2 (24.4-31.6) | 26.8 (24.1-31.0) |
| Medical history | | |
| Previous myocardial infarction | 81 (46.0%) | 65 (37.8%) |
| Previous percutaneous coronary intervention | 74 (42.0%) | 59 (34.3%) |
| Previous coronary artery bypass graft surgery | 34 (19.3%) | 34 (19.8%) |
| Diabetes | 66 (37.5%) | 68 (39.5%) |
| Cerebrovascular accident or transient ischaemic attack | 29 (16.5%) | 39 (22.7%) |
| Atrial fibrillation | 100 (56.8%) | 81 (47.1%) |
| Hypertension | 102 (58.0%) | 98 (57.0%) |
| Months since last heart failure hospitalisation | 3.6 (1.2-6.4) | 3.4 (1.6-6.7) |
| Years since heart failure diagnosis, median | 3.4 (0.8-8.3) | 3.8 (0.9-8.7) |
| Etiology | | |
| Ischaemic | 93 (52.8%) | 81 (47.1%) |
| Heart rate, beats per min | 71 (64-81) | 71 (64-80) |
| Systolic blood pressure, mm Hg | 112 (103-129) | 115 (104-131) |
| Diastolic blood pressure, mm Hg | 68 (60-75) | 68 (61-76) |
| Left ventricular ejection fraction | 30 (23-40) | 30 (22-43) |
| <40% | 127 (72.7%) | 123 (71.5%) |
| ≥40% | 48 (27.3%) | 49 (28.5%) |
| Serum creatinine (µmol/L) | 127 (103-163) | 124 (99-150) |
| eGFR, mL/min | 48 (35-60) | 48 (38-63) |
| Chronic kidney disease (eGFR <60) | 131 (74.4%) | 121 (70.3%) |
| NT-proBNP, pg/mL | 2377 (837-5153) | 1905 (691-4444) |
| Intrinsic cardiac defibrillator | 94 (53.4%) | 102 (59.3%) |
| Cardiac resynchronisation therapy | 46 (26.1%) | 46 (26.7%) |
| Medical therapy | | |
| Beta blocker | 150 (85.2%) | 142 (82.6%) |
| Renin-angiotensin-aldosterone system inhibitor | 154 (87.5%) | 147 (85.5%) |
| Angiotensin-converting enzyme inhibitor | 37 (21.0%) | 32 (18.6%) |
| Angiotensin-receptor blocker | 26 (14.8%) | 26 (15.1%) |
| Angiotensin-receptor neprilysin inhibitor | 81 (46.0%) | 81 (47.1%) |
| Hydralazine dinitrate | 10 (5.7%) | 8 (4.7%) |
| Mineralocorticoid receptor antagonist | 143 (81.3%) | 144 (83.7%) |
| SGLT2 inhibitor | 12 (6.8%) | 21 (12.2%) |

| | | |
|----------------------------|-------------|-------------|
| Loop diuretic | 168 (95.5%) | 167 (97.1%) |
| Thiazide diuretic | 11 (6.3%) | 10 (5.8%) |
| Loop and thiazide diuretic | 11 (6.3%) | 10 (5.8%) |
| Ivabradin | 14 (8.0%) | 10 (5.8%) |
| Digoxin | 44 (25.0%) | 39 (22.7%) |

BMI: body mass index; eGFR: estimated glomerular filtration rate

Table S3. Baseline medical therapy use in HFrEF patients of MONITOR-HF (n=250, intention-to-treat population).

| | PA-guided therapy (n=127) | Standard of Care (n=123) |
|------------------------------------------------|---------------------------|--------------------------|
| Beta blocker | 111 (87.4%) | 101 (82.1%) |
| Renin-angiotensin-aldosterone system inhibitor | 115 (90.6%) | 110 (89.4%) |
| Angiotensin-converting enzyme inhibitor | 25 (19.7%) | 24 (19.5%) |
| Angiotensin-receptor blocker | 17 (13.4%) | 16 (13.0%) |
| Angiotensin-receptor neprilysin inhibitor | 68 (53.5%) | 64 (52.0%) |
| Hydralazine dinitrate | 5 (3.9%) | 6 (4.9%) |
| Mineralocorticoid receptor antagonist | 109 (85.8%) | 106 (86.2%) |
| SGLT2 inhibitor | 11 (8.7%) | 16 (13.0%) |
| Ivabradin | 9 (9.7%) | 9 (7.3%) |
| Digoxin | 34 (26.8%) | 30 (24.4%) |
| Loop diuretic | 122 (96.1%) | 119 (96.7%) |
| Thiazide diuretic | 8 (6.3%) | 8 (6.5%) |
| Loop and thiazide diuretic | 8 (6.3%) | 8 (6.5%) |

Table S4. Detailed overview of quality of life endpoints.

| | n | KCCQ OS at baseline (Cardio MEMS HF system) | KCCQ OS at baseline (Standard Care) | KCCQ OS at 12 months (Cardio MEMS HF system) | KCCQ OS at 12 months (Standard Care) | KCCQ OS mean difference at 12 months (95%CI) (between groups) | P int. | P int. adj. | KCCQ OS mean difference in change between baseline and 12 months (paired analysis) (95%CI) (Cardio MEMS HF system) | KCCQ OS mean difference in change between baseline and 12 months (paired analysis) (95%CI) (Standard Care) | KCCQ OS mean difference in change between baseline and 12 months (95%CI) (between groups) | Number of missing KCCQ values at 12 months (%) | P int. | P int. adj. |
|----------------------|-----|---------------------------------------------|-------------------------------------|----------------------------------------------|--------------------------------------|---------------------------------------------------------------|--------|-------------|--------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|------------------------------------------------|--------|-------------|
| Overall | 279 | 55.8 (23.3) | 54.9 (22.3) | 66.1 (25.4) | 56.9 (24.2) | 9.19 (3.33-15.05) | | | 7.05 (2.77-11.33) | -0.08 (-3.76-3.60) | 7.13 (1.51-12.75) | 69 (19.8) | | |
| Predefined subgroups | | | | | | | | | | | | | | |
| Age ≥69.4 | 131 | 58.1 (22.2) | 53.6 (22.2) | 65.1 (26.1) | 57.5 (24.5) | 7.55 (-1.34-16.45) | 0.61 | 1.00 | 2.56 (-2.50-7.62) | 2.04 (-2.80-6.89) | 0.52 (-6.42-7.45) | 43 (24.7) | 0.03 | 0.33 |
| Age <69.4 | 148 | 53.9 (24.1) | 56.4 (22.6) | 66.8 (25.0) | 56.2 (24.1) | 10.60 (2.62-18.58) | | | 10.36 (3.93-16.78) | -2.29 (-7.93-3.36) | 12.64 (4.16-21.13) | 26 (14.9) | | |
| Female | 74 | 53.2 (22.9) | 49.3 (22.5) | 56.8 (28.0) | 50.9 (25.9) | 5.90 (-6.81-18.6) | 0.56 | 1.00 | 2.31 (-6.18-10.79) | 0.55 (-6.86-7.96) | 1.76 (-9.31-12.83) | 11 (12.9) | 0.27 | 1.00 |
| Male | 205 | 56.6 (23.4) | 57.0 (22.0) | 69.0 (23.9) | 59.2 (23.3) | 9.77 (3.27-16.26) | | | 8.57 (3.57-13.56) | -0.33 (-4.62-3.97) | 8.89 (2.34-15.44) | 58 (22.1) | | |
| Ischemic etiology | 131 | 57.1 (24.5) | 52.6 (22.1) | 67.9 (25.6) | 58.2 (19.9) | 9.63 (1.70-14.56) | 0.86 | 1.00 | 6.18 (-0.22-12.57) | 3.19 (-1.81-8.19) | 2.99 (-5.06-11.03) | 43 (24.7) | 0.18 | 1.00 |

| | | | | | | | | | | | | | | |
|-----------------------|-----|-------------|-------------|-------------|-------------|--------------------|------|------|--------------------|--------------------|---------------------|------------|-------|------|
| Non-ischemic etiology | 148 | 54.5 (21.8) | 56.9 (22.5) | 64.3 (25.2) | 55.8 (27.3) | 8.55 (0.00-17.11) | | | 7.89 (2.03-13.76) | -2.74 (-8.06-2.58) | 10.63 (2.78-18.49) | 26 (14.9) | | |
| LVEF ≥40 | 79 | 56.3 (22.8) | 52.6 (20.7) | 62.9 (27.9) | 51.0 (22.9) | 11.9 (0.17-23.65) | 0.52 | 1.00 | 3.12 (-4.99-11.23) | -2.09 (-7.34-3.17) | 5.20 (-4.32-14.73) | 18 (18.6) | 0.71 | 1.00 |
| LVEF <40 | 200 | 55.8 (23.6) | 55.8 (23.0) | 67.2 (24.5) | 59.5 (24.5) | 7.69 (0.86-14.52) | | | 8.41 (3.33-13.5) | 0.81 (-4.01-5.63) | 7.60 (0.64-14.56) | 50 (20.0) | | |
| AF | 141 | 57.7 (24.1) | 54.3 (23.0) | 64.3 (26.4) | 55.7 (24.8) | 8.57 (0.05-17.08) | 0.77 | 1.00 | 2.84 (-2.70-8.38) | 0 (-6.06-6.05) | 2.84 (-5.30-10.98) | 40 (22.1) | 0.10 | 0.80 |
| No AF | 138 | 53.4 (22.1) | 55.4 (21.9) | 68.2 (24.2) | 57.9 (23.8) | 10.3 (2.13-18.47) | | | 12.10 (5.49-18.71) | -0.14 (-4.68-4.40) | 12.24 (4.29-20.20) | 29 (17.4) | | |
| DM | 105 | 56.0 (25.2) | 50.7 (21.7) | 63.6 (25.5) | 57.0 (25.9) | 6.61 (-3.41-16.63) | 0.52 | 1.00 | 3.09 (-4.92-11.11) | 6.16 (0.49-11.83) | -3.06 (-12.77-6.65) | 29 (21.6) | 0.005 | 0.06 |
| No DM | 174 | 55.7 (22.2) | 57.6 (22.5) | 67.4 (25.4) | 56.8 (23.2) | 10.58 (3.30-17.86) | | | 9.16 (4.12-14.21) | -4.26 (-8.98-0.47) | 13.42 (6.56-20.28) | 40 (18.7) | | |
| CRT | 72 | 57.0 (21.9) | 55.3 (20.4) | 60.8 (25.2) | 56.1 (25.0) | 4.69 (-7.10-16.48) | 0.38 | 1.00 | 0.73 (-7.20-8.67) | -1.68 (-9.39-6.03) | 2.41 (-8.45-13.28) | 20 (21.7) | 0.32 | 1.00 |
| No CRT | 206 | 55.4 (23.8) | 54.9 (23.1) | 68.0 (25.3) | 57.4 (24.0) | 10.61 (3.81-17.41) | | | 9.42 (4.34-14.50) | 0.56 (-3.73-4.84) | 8.86 (2.26-15.47) | 49 (19.2) | | |
| ICD | 160 | 56.9 (22.6) | 57.1 (21.4) | 65.7 (25.2) | 58.6 (24.1) | 7.10 (-0.65-14.84) | 0.40 | 1.00 | 7.75 (1.83-13.66) | -1.49 (-6.26-3.27) | 9.24 (1.70-16.78) | 36 (18.4%) | 0.38 | 1.00 |
| No ICD | 119 | 54.6 (24.1) | 51.7 (23.4) | 66.5 (25.8) | 54.4 (24.4) | 12.15 (3.03-21.27) | | | 6.18 (-0.18-12.55) | 1.97 (-3.95-7.90) | 4.21 (-4.39-12.81) | 33 (21.7) | | |
| Exploratory subgroups | | | | | | | | | | | | | | |
| eGFR ≥60 | 81 | 56.9 (22.9) | 53.1 (24.9) | 64.2 (24.2) | 59.9 (23.7) | 4.25 (-6.42-14.92) | 0.29 | 1.00 | 8.17 (1.23-15.12) | 3.66 (-2.75-10.07) | 4.51 (-4.79-13.82) | 14 (14.7) | 0.55 | 1.00 |

| | | | | | | | | | | | | | | |
|-----------------|-----|-------------|-------------|-------------|-------------|---------------------|------|------|--------------------|--------------------|---------------------|-----------|------|------|
| eGFR <60 | 198 | 55.5 (23.5) | 55.7 (21.2) | 66.8 (25.9) | 55.6 (24.4) | 11.23 (4.16-18.3) | | | 6.61 (1.25-11.98) | -1.67 (-6.19-2.85) | 8.28 (1.31-15.26) | 55 (21.7) | | |
| Obesity | 91 | 51.5 (21.6) | 53.2 (22.6) | 64.4 (25.8) | 53.4 (24.6) | 10.98 (0.40-21.57) | 0.66 | 1.00 | 7.76 (0.64-14.89) | -0.05 (-7.10-7.00) | 7.81 (-2.07-17.70) | 21 (18.8) | 0.87 | 1.00 |
| No obesity | 188 | 58.0 (23.9) | 55.6 (22.3) | 66.8 (25.3) | 58.6 (24.0) | 8.16 (1.06-15.26) | | | 6.73 (1.33-12.13) | -0.09 (-4.42-4.24) | 6.82 (-0.06-13.70) | 48 (20.3) | | |
| GDMT ≥3 | 144 | 57.5 (21.4) | 58.6 (21.8) | 67.9 (23.7) | 59.0 (24.9) | 8.91 (0.90-16.93) | 0.55 | 1.00 | 8.11 (2.51-13.71) | -1.77 (-7.46-3.91) | 9.88 (1.97-17.80) | 23 (13.8) | 0.40 | 1.00 |
| GDMT <3 | 56 | 51.7 (28.2) | 51.1 (24.4) | 64.7 (27.4) | 60.4 (23.9) | 4.24 (-10.02-18.50) | | | 9.41 (-3.13-21.94) | 6.22 (-2.92-15.35) | 3.19 (-11.98-18.36) | 27 (32.5) | | |
| NTproB NP ≥2146 | 119 | 53.6 (23.0) | 53.3 (21.5) | 64.1 (25.7) | 55.5 (23.3) | 8.60 (-0.32-17.51) | 0.97 | 1.00 | 7.38 (0.09-14.66) | -0.31 (-6.70-6.09) | 7.69 (-1.91-17.28) | 43 (26.5) | 0.85 | 1.00 |
| NTproB NP <2146 | 138 | 57.7 (22.6) | 57.5 (22.5) | 67.0 (25.4) | 58.6 (25.4) | 8.38 (-0.26-17.01) | | | 6.02 (0.80-11.24) | -0.57 (-5.11-3.98) | 6.59 (-0.27-13.44) | 24 (14.8) | | |

KCCQ OS: Kansas City Cardiomyopathy Questionnaire overall summary score; P int: P interaction; P int adj: Pinteraction adjusted; LVEF: left ventricular ejection fraction; AF: atrial fibrillation; DM: diabetes mellitus; CRT: cardiac resynchronization therapy; ICD: implantable cardiac defibrillator; eGFR: estimated glomerular filtration rate; GDMT: guideline-directed medical therapy; HFREF: heart failure with a reduced ejection fraction.

Table S5. Detailed overview of clinical endpoints.

| | n | Total HFH (rate/pty) (CardioME MS HF system) | Total HFH (rate/pty) (Standard Care) | Total HFH HR (95% CI) | P int. | P int. adj. | Total HFH and all- cause mortality (rate/pty) (CardioME MS HF system) | Total HFH and all- cause mortality (rate/pty) (Standard Care) | Total HFH and all- cause mortality HR (95% CI) | P int. | P int. adj. |
|------------------------------|-----|----------------------------------------------------------|-----------------------------------------------|-----------------------------|--------|-------------|--------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------|--------|-------------|
| Overall | 348 | 117 (0.38) | 212 (0.68) | 0.56 (0.38-0.84) | | | 159 (0.52) | 257 (0.82) | 0.63 (0.44-0.90) | | |
| Predefined subgroups | | | | | | | | | | | |
| Age ≥69.4 | 174 | 45 (0.33) | 85 (0.52) | 0.64 (0.38-1.08) | 0.50 | 1.00 | 66 (0.48) | 116 (0.71) | 0.70 (0.45-1.09) | 0.60 | 1.00 |
| Age <69.4 | 174 | 72 (0.42) | 127 (0.85) | 0.49 (0.28-0.87) | | | 93 (0.55) | 141 (0.94) | 0.58 (0.34-0.97) | | |
| Female | 85 | 27 (0.36) | 65 (0.72) | 0.51 (0.28-0.94) | 0.74 | 1.00 | 33 (0.44) | 73 (0.80) | 0.56 (0.30-1.02) | 0.67 | 1.00 |
| Male | 263 | 90 (0.39) | 147 (0.66) | 0.58 (0.36-0.96) | | | 126 (0.54) | 184 (0.83) | 0.65 (0.43-1.00) | | |
| Ischemic etiology | 174 | 75 (0.48) | 76 (0.54) | 0.89 (0.52-1.55) | 0.02 | 0.24 | 104 (0.66) | 102 (0.72) | 0.93 (0.58-1.47) | 0.02 | 0.24 |
| Non- ischemic etiology | 174 | 42 (0.28) | 136 (0.80) | 0.36 (0.22-0.59) | | | 55 (0.37) | 155 (0.91) | 0.41 (0.25-0.67) | | |
| LVEF ≥40 | 97 | 33 (0.50) | 63 (0.69) | 0.70 (0.40-1.23) | 0.42 | 1.00 | 44 (0.67) | 71 (0.78) | 0.84 (0.50-1.41) | 0.30 | 1.00 |
| LVEF <40 | 250 | 84 (0.35) | 149 (0.68) | 0.53 (0.31-0.88) | | | 114 (0.47) | 186 (0.84) | 0.57 (0.37-0.90) | | |
| AF | 181 | 72 (0.40) | 108 (0.77) | 0.54 (0.34-0.88) | 0.89 | 1.00 | 95 (0.53) | 129 (0.92) | 0.60 (0.39-0.93) | 0.76 | 1.00 |
| No AF | 167 | 45 (0.35) | 104 (0.60) | 0.57 (0.28-1.18) | | | 64 (0.50) | 128 (0.74) | 0.67 (0.37-1.23) | | |
| DM | 134 | 34 (0.32) | 96 (0.73) | 0.42 (0.23-0.77) | 0.27 | 1.00 | 57 (0.53) | 118 (0.90) | 0.58 (0.35-0.97) | 0.67 | 1.00 |
| No DM | 214 | 83 (0.42) | 116 (0.64) | 0.67 (0.40-1.12) | | | 102 (0.51) | 139 (0.77) | 0.68 (0.43-1.09) | | |

| | | | | | | | | | | | |
|-----------------------|-----|-----------|------------|------------------|------|------|------------|------------|------------------|------|------|
| CRT | 92 | 42 (0.48) | 74 (1.05) | 0.54 (0.23-1.24) | 0.66 | 1.00 | 52 (0.60) | 93 (1.32) | 0.52 (0.25-1.10) | 0.33 | 1.00 |
| No CRT | 255 | 75 (0.34) | 136 (0.56) | 0.60 (0.39-0.91) | | | 107 (0.49) | 162 (0.67) | 0.72 (0.49-1.04) | | |
| ICD | 196 | 76 (0.43) | 143 (0.76) | 0.57 (0.33-0.98) | 1.00 | 1.00 | 97 (0.54) | 171 (0.90) | 0.61 (0.38-0.99) | 0.70 | 1.00 |
| No ICD | 152 | 41 (0.32) | 69 (0.56) | 0.57 (0.33-0.97) | | | 62 (0.48) | 86 (0.70) | 0.69 (0.43-1.11) | | |
| Exploratory subgroups | | | | | | | | | | | |
| eGFR \geq 60 | 95 | 19 (0.23) | 55 (0.58) | 0.40 (0.16-0.99) | 0.43 | 1.00 | 23 (0.28) | 65 (0.69) | 0.41 (0.17-0.97) | 0.28 | 1.00 |
| eGFR <60 | 253 | 98 (0.44) | 157 (0.72) | 0.61 (0.39-0.95) | | | 136 (0.61) | 192 (0.88) | 0.69 (0.47-1.02) | | |
| Obesity | 112 | 23 (0.26) | 63 (0.60) | 0.41 (0.22-0.77) | 0.34 | 1.00 | 37 (0.42) | 70 (0.67) | 0.61 (0.35-1.05) | 0.92 | 1.00 |
| No obesity | 236 | 94 (0.43) | 149 (0.72) | 0.61 (0.38-1.01) | | | 122 (0.56) | 187 (0.90) | 0.63 (0.41-0.98) | | |
| GDMT \geq 3 | 167 | 54 (0.32) | 87 (0.60) | 0.53 (0.26-1.06) | 0.92 | 1.00 | 72 (0.42) | 101 (0.70) | 0.61 (0.33-1.12) | 0.93 | 1.00 |
| GDMT <3 | 83 | 30 (0.44) | 64 (0.82) | 0.53 (0.27-1.06) | | | 42 (0.61) | 85 (1.09) | 0.56 (0.30-1.04) | | |
| NTproBNP \geq 2146 | 162 | 54 (0.39) | 116 (0.93) | 0.42 (0.25-0.70) | 0.12 | 1.00 | 82 (0.59) | 143 (1.14) | 0.51 (0.32-0.82) | 0.16 | 1.00 |
| NTproBNP <2146 | 162 | 52 (0.40) | 80 (0.48) | 0.82 (0.42-1.58) | | | 66 (0.50) | 94 (0.57) | 0.89 (0.49-1.59) | | |

HFH: heart failure hospitalization; pty: patient-year; HR: hazard ratio; P int: P interaction; P int adj: P interaction adjusted; LVEF: left ventricular ejection fraction; AF: atrial fibrillation; DM: diabetes mellitus; CRT: cardiac resynchronization therapy; ICD: implantable cardiac defibrillator; eGFR: estimated glomerular filtration rate; GDMT: guideline-directed medical therapy; HFrEF: heart failure with a reduced ejection fraction.

Table S5. Detailed overview of clinical endpoints (continued).

| | n | Time to first HFH (rate) CardioME MS HF system | Time to first HFH (rate) Standard Care | Time to first HFH HR (95% CI) | P int. | P int. adj. | Time to first HFH or CV mortality (rate) (CardioME MS HF system) | Time to first HFH or CV mortality (rate) (Standard Care) | Time to first HFH or CV mortality HR (95% CI) | P int. | P int. adj. |
|-----------------------|-----|------------------------------------------------|----------------------------------------|-------------------------------|--------|-------------|------------------------------------------------------------------|----------------------------------------------------------|-----------------------------------------------|--------|-------------|
| Overall | 348 | 63 (0.25) | 85 (0.40) | 0.67 (0.49-0.93) | | | 71 (0.29) | 91 (0.42) | 0.71 (0.52-0.97) | | |
| Predefined subgroups | | | | | | | | | | | |
| Age ≥69.4 | 174 | 15 (0.14) | 22 (0.18) | 0.82 (0.51-1.32) | 0.22 | 1.00 | 34 (0.31) | 47 (0.38) | 0.86 (0.56-1.34) | 0.20 | 1.00 |
| Age <69.4 | 174 | 25 (0.18) | 25 (0.28) | 0.55 (0.35-0.86) | | | 37 (0.27) | 44 (0.49) | 0.58 (0.38-0.90) | | |
| Female | 85 | 16 (0.26) | 26 (0.44) | 0.64 (0.35-1.21) | 0.91 | 1.00 | 17 (0.28) | 26 (0.44) | 0.69 (0.37-1.27) | 0.95 | 1.00 |
| Male | 263 | 47 (0.25) | 59 (0.38) | 0.69 (0.47-1.01) | | | 54 (0.29) | 65 (0.42) | 0.72 (0.50-1.03) | | |
| Ischemic etiology | 174 | 34 (0.28) | 37 (0.34) | 0.83 (0.52-1.32) | 0.27 | 1.00 | 41 (0.34) | 43 (0.39) | 0.86 (0.56-1.32) | 0.24 | 1.00 |
| Non-ischemic etiology | 174 | 29 (0.23) | 48 (0.45) | 0.58 (0.36-0.91) | | | 30 (0.24) | 48 (0.45) | 0.60 (0.38-0.94) | | |
| LVEF ≥40 | 97 | 19 (0.36) | 29 (0.50) | 0.74 (0.41-1.32) | 0.81 | 1.00 | 20 (0.38) | 29 (0.50) | 0.78 (0.44-1.38) | 0.75 | 1.00 |
| LVEF <40 | 250 | 44 (0.23) | 56 (0.36) | 0.67 (0.45-1.00) | | | 50 (0.26) | 62 (0.40) | 0.69 (0.48-1.00) | | |
| AF | 181 | 41 (0.30) | 45 (0.47) | 0.69 (0.45-1.05) | 0.78 | 1.00 | 46 (0.33) | 46 (0.48) | 0.76 (0.50-1.14) | 0.57 | 1.00 |
| No AF | 167 | 22 (0.20) | 40 (0.34) | 0.61 (0.36-1.03) | | | 25 (0.23) | 45 (0.38) | 0.62 (0.38-1.01) | | |
| DM | 134 | 23 (0.26) | 38 (0.44) | 0.60 (0.36-1.01) | 0.54 | 1.00 | 27 (0.31) | 40 (0.46) | 0.67 (0.41-1.09) | 0.73 | 1.00 |
| No DM | 214 | 40 (0.25) | 47 (0.37) | 0.74 (0.48-1.13) | | | 44 (0.28) | 51 (0.40) | 0.75 (0.50-1.12) | | |

| | | | | | | | | | | | |
|-----------------------|-----|-----------|-----------|------------------|------|------|-----------|-----------|------------------|------|------|
| CRT | 92 | 19 (0.28) | 25 (0.52) | 0.62 (0.34-1.14) | 0.62 | 1.00 | 21 (0.31) | 27 (0.56) | 0.64 (0.36-1.13) | 0.53 | 1.00 |
| No CRT | 255 | 44 (0.24) | 59 (0.35) | 0.71 (0.48-1.05) | | | 50 (0.28) | 63 (0.38) | 0.76 (0.52-1.10) | | |
| ICD | 196 | 39 (0.29) | 52 (0.39) | 0.75 (0.50-1.14) | 0.45 | 1.00 | 43 (0.32) | 55 (0.42) | 0.79 (0.53-1.17) | 0.48 | 1.00 |
| No ICD | 152 | 24 (0.21) | 33 (0.40) | 0.57 (0.34-0.97) | | | 28 (0.25) | 36 (0.43) | 0.62 (0.37-1.01) | | |
| Exploratory subgroups | | | | | | | | | | | |
| eGFR \geq 60 | 95 | 8 (0.11) | 22 (0.34) | 0.34 (0.15-0.77) | 0.07 | 0.84 | 9 (0.12) | 23 (0.35) | 0.37 (0.17-0.80) | 0.06 | 0.72 |
| eGFR <60 | 253 | 55 (0.32) | 63 (0.42) | 0.79 (0.55-1.13) | | | 62 (0.36) | 68 (0.45) | 0.82 (0.58-1.16) | | |
| Obesity | 112 | 15 (0.19) | 28 (0.42) | 0.46 (0.25-0.87) | 0.16 | 1.00 | 19 (0.24) | 28 (0.42) | 0.59 (0.33-1.05) | 0.44 | 1.00 |
| No obesity | 236 | 48 (0.28) | 57 (0.38) | 0.79 (0.53-1.15) | | | 52 (0.31) | 63 (0.42) | 0.77 (0.53-1.12) | | |
| GDMT \geq 3 | 167 | 27 (0.19) | 32 (0.30) | 0.66 (0.39-1.10) | 0.82 | 1.00 | 32 (0.23) | 36 (0.34) | 0.70 (0.43-1.12) | 0.96 | 1.00 |
| GDMT <3 | 83 | 17 (0.32) | 24 (0.48) | 0.74 (0.40-1.39) | | | 18 (0.34) | 26 (0.51) | 0.73 (0.40-1.33) | | |
| NTproBNP \geq 2146 | 162 | 32 (0.27) | 39 (0.46) | 0.61 (0.38-0.97) | 0.49 | 1.00 | 38 (0.32) | 43 (0.51) | 0.66 (0.42-1.02) | 0.57 | 1.00 |
| NTproBNP <2146 | 162 | 24 (0.24) | 38 (0.31) | 0.77 (0.46-1.29) | | | 26 (0.26) | 40 (0.33) | 0.80 (0.49-1.31) | | |

HFH: heart failure hospitalization; CV: cardiovascular; pty: patient-year; HR: hazard ratio; P int: P interaction; P int adj: P interaction adjusted; LVEF: left ventricular ejection fraction; AF: atrial fibrillation; DM: diabetes mellitus; CRT: cardiac resynchronization therapy; ICD: implantable cardiac defibrillator; eGFR: estimated glomerular filtration rate; GDMT: guideline-directed medical therapy; HF_rEF: heart failure with a reduced ejection fraction.

Table S6. Detailed overview of pulmonary artery pressure endpoints.

| | n | Mean PAP AUC at 12 months | P int. | P int. adj. | mPAP at baseline | mPAP at 12 months | mPAP mean change (paired analysis) (95%CI) | P int. | P int. adj. |
|--------------------------|-----|---------------------------------|--------|-------------|---------------------|----------------------|-----------------------------------------------------|--------|-------------|
| Overall | 168 | -1624 (2003) | | | 33.3 (10.6) | 24.9 (9.4) | -6.46 (-7.97- - 4.94) | | |
| Predefined subgroups | | | | | | | | | |
| Age ≥69.4 | 74 | -1728 (1971) | 0.55 | 1.00 | 35.4 (9.89) | 27.6 (9.89) | -6.59 (-9.10- - 4.08) | 0.89 | 1.00 |
| Age <69.4 | 94 | -1543 (2035) | | | 31.6 (10.9) | 23.0 (8.51) | -6.36 (-8.29- - 4.43) | | |
| Female | 37 | -1094 (1540) | 0.03 | 0.33 | 30.8 (11.6) | 25.1 (10.3) | -3.86 (-5.79- - 1.93) | 0.01 | 0.12 |
| Male | 131 | -1775 (2097) | | | 34.0 (10.3) | 24.9 (9.12) | -7.25 (-9.13 - - 5.38) | | |
| Ischemic etiology | 88 | -1636 (2074) | 0.93 | 1.00 | 35.0 (10.9) | 25.8 (8.96) | -6.44 (-8.73- - 4.15) | 0.98 | 1.00 |
| Non-ischemic etiology | 80 | -1610 (1934) | | | 31.4 (10.0) | 24.0 (9.77) | -6.48 (-8.52- - 4.44) | | |
| LVEF ≥40 | 46 | -1104 (1703) | 0.02 | 0.24 | 32.6 (9.82) | 25.7 (8.69) | -4.32 (-7.07 - - 1.57) | 0.08 | 0.80 |
| LVEF <40 | 121 | -1830 (2079) | | | 33.4 (10.9) | 24.7 (9.62) | -7.18 (-8.98- - 5.37) | | |
| AF | 95 | -1576 (1908) | 0.73 | 1.00 | 34.6 (9.85) | 26.7 (9.59) | -6.11 (-8.11- - 4.12) | 0.62 | 1.00 |
| No AF | 73 | -1686 (2131) | | | 31.6 (11.4) | 22.6 (8.63) | -6.9 (-9.30- - 4.50) | | |
| DM | 61 | -1778 (1959) | 0.45 | 1.00 | 34.5 (9.42) | 27.0 (8.95) | -5.63 (-8.07- - 3.19) | 0.42 | 1.00 |
| No DM | 107 | -1535 (2032) | | | 32.6 (11.2) | 23.8 (9.46) | -6.90 (-8.86- - 4.94) | | |
| CRT | 45 | -1493 (1956) | 0.60 | 1.00 | 33.0 (9.34) | 25.8 (8.47) | -5.89 (-8.73- - 3.05) | 0.65 | 1.00 |
| No CRT | 123 | -1672 (2027) | | | 33.4 (11.1) | 24.6 (9.69) | -6.66 (-8.48- - 4.84) | | |

| | | | | | | | | | |
|-----------------------|-----|--------------|--------|-------|-------------|-------------|-----------------------|--------|-------|
| ICD | 92 | -1722 (1985) | 0.49 | 1.00 | 33.6 (10.2) | 24.4 (8.59) | -7.31 (-9.49- -5.14) | 0.23 | 1.00 |
| No ICD | 76 | -1503 (2033) | | | 32.9 (11.2) | 25.5 (10.2) | -5.46 (-7.58- -3.33) | | |
| Exploratory subgroups | | | | | | | | | |
| Baseline mPAP >25 | 93 | -2112 (2295) | 0.0002 | 0.003 | 39.6 (7.88) | 29.3 (8.72) | -9.18 (-11.72- -6.64) | 0.0004 | 0.006 |
| Baseline mPAP ≤25 | 69 | -987 (1376) | | | 25.0 (8.22) | 20.8 (8.38) | -3.56 (-5.24- -1.87) | | |
| eGFR ≥60 | 43 | -1374 (1541) | 0.27 | 1.00 | 27.8 (10.5) | 20.6 (8.26) | -5.04 (-6.90- -3.18) | 0.15 | 1.00 |
| eGFR <60 | 125 | -1711 (2139) | | | 35.2 (10.0) | 26.7 (9.26) | -7.03 (-9.02- -5.03) | | |
| Obesity | 54 | -1428 (1756) | 0.36 | 1.00 | 32.8 (9.94) | 27.1 (7.27) | -4.08 (-6.22- -1.93) | 0.02 | 0.22 |
| No obesity | 114 | -1715 (2110) | | | 33.5 (10.9) | 24.0 (10.0) | -7.46 (-9.39- -5.52) | | |
| GDMT ≥3 | 88 | 1734 (2014) | 0.43 | 1.00 | 32.5 (10.8) | 24.3 (8.73) | -6.52 (-8.52- -4.51) | 0.26 | 1.00 |
| GDMT <3 | 33 | 2088 (2257) | | | 35.8 (11.0) | 25.7 (12.0) | -9.09 (-13.27- -4.93) | | |
| NTproBNP ≥2146 | 82 | -2183 (2166) | 0.001 | 0.01 | 37.2 (9.41) | 26.3 (8.54) | -9.15 (-11.45- -6.84) | 0.003 | 0.04 |
| NTproBNP <2146 | 73 | -1147 (1767) | | | 29.5 (11.0) | 23.1 (10.2) | -4.38 (-6.55- -2.22) | | |
| PVR >2 | 65 | -2038 (2087) | 0.09 | 0.90 | 37.5 (9.25) | 27.6 (8.46) | -8.49 (-10.94- -6.05) | 0.11 | 0.99 |
| PVR ≤2 | 88 | -1462 (2000) | | | 30.5 (10.2) | 23.2 (9.67) | -5.85 (-8.03- -3.68) | | |

PAP AUC: pulmonary artery pressure area under the curve (mmHg.days); mPAP: mean pulmonary artery pressure (mmHg); 12M: 12 months; P int: P interaction; P int adj: P interaction adjusted; LVEF: left ventricular ejection fraction; AF: atrial fibrillation; DM: diabetes mellitus; CRT: cardiac resynchronization therapy; ICD: implantable cardiac defibrillator; eGFR: estimated glomerular filtration rate; GDMT: guideline-directed medical therapy; HFrEF: heart failure with a reduced ejection fraction; PVR: peripheral vascular resistance.