**Supplementary Material**

# Efficacy and Safety of Esaxerenone in Hypertensive Patients with Left Ventricular Hypertrophy (ESES-LVH) Study: A Multicenter, Open-Label, Prospective, Interventional Study

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**Supplementary Materials**

**Table S1.** List of participating institutions and representative physicians[a]

| Institution | Representative physicians |
|---|---|
| Kumamoto University Hospital | Shinsuke Hanatani, Kyoko Hirakawa, Kenichi Matsushita, Taishi Nakamura, Daisuke Sueta, Satoru Suzuki, Seiji Takashio, Kenichi Tsujita (principal investigator), Eiichiro Yamamoto |
| Amakusa Medical Center | Shinsuke Hanatani, Yasuhiro Nagayoshi, Taiki Nishihara, Naritsugu Sakaino |
| Arao Municipal Hospital | Shunichiro Fuchigami, Shinsuke Hanatani, Ichiro Kajiwara, Nobuhiro Nakanishi, Daisuke Sueta, Satoru Yamamura |
| Higashi Diabetes and Cardiovascular Clinic | Takayuki Higashi |
| Hirayama Heart Clinic | Kazuto Hirayama, Touitsu Hirayama |
| Hitoyoshi Medical Center | Yusuke Kanemaru, Hirofumi Kurokawa, Shinichi Nakamura, Yoshiro Onoue, Taku Rokutanda, Takayoshi Yamashita |
| Jinnouchi Hospital | Kunio Hieshima, Hideaki Jinnouchi, Katsunori Jinnouchi, Keizo Kajiwara, Noboru Kurinami, Seigo Sugiyama, Tomoko Suzuki |
| Kanoya Heart Center | Hidekazu Arai |
| Kumamoto Chuo Hospital | Shunichiro Fuchigami, Eiji Horio, Kenji Morihisa, Hisato Nako, Tsunenori Nishijima, Katsuo Noda, Taku Rokutanda, Yuichiro Tsuruta |

| | |
|---|---|
| Kumamoto City Hospital | Ikuo Misumi, Miwa Nagano, Koji Sato |
| Kumamoto Kenhoku Hospital | Masakazu Matsukawa, Hisato Nako, Takanori Tokitsu |
| Kumamoto Rosai Hospital | Koji Abe, Hideki Doi, Shotaro Furukawa, Daiki Kakumori, Kazunobu Kawakami, Toshiyuki Matsumura, Kota Motozato |
| Minamata City General Hospital & Medical Center | Toyoki Hirose, Tomoaki Uemura |
| Miyazaki Prefectural Nobeoka Hospital | So Ikebe, Masanobu Ishii, Ryota Kaichi, Soichi Komaki, Kazumasa Kuroki, Hiroaki Kusaka, Takayuki Mori, Masafumi Takae, Nobuyasu Yamamoto |
| Nakayama Cardiovascular Clinic | Masafumi Nakayama |
| National Hospital Organization Kumamoto Medical Center | Kazuteru Fujimoto, Yuichi Kimura, Hiroaki Kusaka, Junichi Matsubara, Takumi Nagakura, Atsushi Nozuhara, Yasuhiro Otsuka, Shinji Tayama |
| Nishinihon Hospital | Yuichiro Arima, Tomoko Iwasaki |
| Sakanashi Heart Clinic | Masaki Goto, Yasuyuki Hanada, Toshihiko Sakanashi |
| Shinbeppu Hospital | Koichi Kikuta, Mitsutoshi Miura, Takashi Miyazaki, Suguru Nagamatsu, Keisuke Watanabe |
| Yatsushiro Heart Clinic | Hideo Takashima |

[a]Institutions and investigators are listed in alphabetical order except for Kumamoto

University Hospital, where the principal investigator belongs. The facility representatives are underlined.

**Table S2**. Detailed inclusion and exclusion criteria

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|---|
| **Main inclusion criteria**<br>1) Patients aged ≥ 20 years who had been taking a RASi or a CCB at a fixed dosage regimen from 28 days or earlier before the start of esaxerenone administration<br>2) Mean sitting home SBP of 135 to ≤ 159 mmHg and/or DBP of 85 to ≤ 99 mmHg using an upper arm cuff sphygmomanometer in the past 5 days or more prior to the registration date and within 14 days before the start of esaxerenone administration<br>3) Patients with LVH who met any of the following criteria:<br>a) Thickening of the left ventricular posterior wall or intraventricular septal wall of ≥ 12 mm on echocardiogram<br>b) LVH with Sv1 + Rv5 ≥ 35 mm on electrocardiogram<br>c) LVMI ≥ 125 g/m$^2$ for men and ≥ 110 g/m$^2$ for women |
| **Main exclusion criteria**<br>1) Secondary hypertension or malignant hypertension<br>2) Type 1 diabetes mellitus<br>3) Complication or history of orthostatic hypotension<br>4) Complication or history of cerebrocardiovascular disease that corresponds to any of the following:<br>a) Patients who developed myocardial infarction, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, |

or stroke of unknown type (TIA can be registered) within 6 months before written consent was obtained

b) Patients who had undergone procedures such as PCI, CABG, or ablation within 6 months before written consent was obtained

c) Patients scheduled to undergo procedures such as PCI, CABG, or ablation at the start of treatment

d) Patients with heart failure and LVEF that decreased to < 50%

e) Patients diagnosed with idiopathic cardiomyopathy

f) Patients with current or history of congenital or rheumatic heart disease

g) Patients with unstable angina, severe arrhythmia (e.g., life-threatening refractory ventricular arrhythmias or arrhythmias with irregular R-R intervals such as sick sinus syndrome)

5) Patients with symptoms or contraindications for treatment with esaxerenone as indicated in the esaxerenone package insert, such as hyperkalemia, serum potassium level ≥ 5.0 mEq/l, or severe renal impairment with eGFRcreat < 30 ml/min/1.73 $m^2$

*CABG* coronary artery bypass grafting, *CCB* calcium channel blocker, *DBP* diastolic blood pressure, *eGFRcreat* creatinine-based estimated glomerular filtration rate, *LVEF* left ventricular ejection fraction, *LVH* left ventricular hypertrophy, *LVMI* left ventricular mass index, *PCI* percutaneous coronary intervention, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure, *TIA* transient ischemic attack

**Table S3**. Change from baseline in BP (full analysis set)

| | Total *N* = 58 | | Subcohorts | | | |
|---|---|---|---|---|---|---|
| | | | RASi *n* = 19 | | CCB *n* = 39 | |
| | SBP, mmHg | DBP, mmHg | SBP, mmHg | DBP, mmHg | SBP, mmHg | DBP, mmHg |
| **Morning home BP** | | | | | | |
| **Baseline, *n*** | 58 | 58 | 19 | 19 | 39 | 39 |
| Mean ± SD | 142.8 ± 8.1 | 85.0 ± 10.0 | 142.7 ± 8.4 | 86.3 ± 7.1 | 142.8 ± 8.1 | 84.4 ± 11.2 |
| **Week 2, *n*** | 52 | 52 | 16 | 16 | 36 | 36 |
| Mean ± SD | 135.9 ±11.0 | 82.8 ± 10.3 | 135.6 ±13.1 | 83.6 ± 8.8 | 136.1 ± 10.1 | 82.5 ± 10.9 |
| Change from baseline | −6.7 ± 9.0*** | −2.5 ± 5.6** | −7.0 ± 10.7* | −3.3 ± 6.5 | −6.5 ± 8.3*** | −2.2 ± 5.2* |
| **Week 4, *n*** | 57 | 57 | 18 | 18 | 39 | 39 |
| Mean ± SD | 134.7 ±9.8 | 81.9 ± 9.9 | 135.8 ± 11.4 | 82.1 ± 7.5 | 134.2 ± 9.0 | 81.8 ± 10.9 |
| Change from baseline | −8.2 ± 8.1*** | −3.1 ± 5.0*** | −7.3 ± 7.2*** | −4.2 ± 5.3** | −8.6 ± 8.5*** | −2.6 ± 4.8** |
| **Week 6, *n*** | 56 | 56 | 18 | 18 | 38 | 38 |
| Mean ± SD | 131.7 ± 9.2 | 80.2 ± 9.3 | 133.7 ± 11.4 | 81.8 ± 7.9 | 130.8 ± 7.9 | 79.4 ± 10.0 |
| Change from baseline | −10.9 ± 9.6*** | −4.5 ± 6.3*** | −9.4 ± 10.0*** | −4.4 ± 7.7* | −11.6 ± 9.5*** | −4.6 ± 5.6*** |
| **Week 8, *n*** | 57 | 57 | 18 | 18 | 39 | 39 |
| Mean ± SD | 131.8 ± 9.4 | 80.4 ± 9.2 | 133.4 ± 12.5 | 80.7 ± 7.6 | 131.1 ± 7.6 | 80.2 ± 9.9 |
| Change from baseline | −11.1 ± 9.8*** | −4.6 ± 6.3*** | −9.6 ± 10.7** | −5.5 ± 7.3** | −11.7 ± 9.4*** | −4.2 ± 5.9*** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Week 10, *n*** | 55 | 55 | 17 | 17 | 38 | 38 |
| Mean ± SD | 130.9 ± 9.3 | 80.0 ± 9.3 | 131.8 ± 11.2 | 80.1 ± 7.2 | 130.5 ± 8.5 | 80.0 ± 10.2 |
| Change from baseline | −11.5 ± 9.6*** | −4.5 ± 6.3*** | −10.6 ± 7.9*** | −5.5 ± 4.7*** | −11.9 ± 10.3*** | −4.0 ± 6.9*** |
| **Week 12, *n*** | 56 | 56 | 18 | 18 | 38 | 38 |
| Mean ± SD | 132.1 ± 12.0 | 79.9 ± 9.9 | 133.7 ± 13.7 | 79.6 ± 7.8 | 131.4 ± 11.2 | 80.1 ± 10.9 |
| Change from baseline | −10.5 ± 11.8*** | −4.8 ± 7.5*** | −9.4 ± 11.0** | −6.7 ± 8.2** | −11.0 ± 12.2*** | −3.9 ± 7.0** |
| **Week 24, *n*** | 55 | 55 | 17 | 17 | 38 | 38 |
| Mean ± SD | 130.9 ± 11.2 | 80.2 ± 10.4 | 129.5 ± 12.9 | 78.4 ± 8.1 | 131.5 ± 10.5 | 81.0 ± 11.3 |
| Change from baseline | −11.9 ± 12.0*** | −5.0 ± 7.6*** | −13.2 ± 9.9*** | −7.9 ± 7.1*** | −11.4 ± 12.9*** | −3.8 ± 7.6** |
| **EOT, *n*** | 58 | 58 | 19 | 19 | 39 | 39 |
| Mean ± SD | 131.2 ± 12.0 | 80.3 ± 10.5 | 131.1 ± 15.0 | 79.6 ± 8.6 | 131.3 ± 10.5 | 80.6 ± 11.4 |
| Change from baseline | −11.5 ± 12.3*** | −4.7 ± 7.7*** | −11.6 ± 11.7*** | −6.6 ± 7.9** | −11.5 ± 12.8*** | −3.8 ± 7.5** |
| **Bedtime home BP** | | | | | | |
| **Baseline, *n*** | 58 | 58 | 19 | 19 | 39 | 39 |
| Mean ± SD | 141.0 ± 8.4 | 81.9 ± 10.5 | 140.1 ± 8.5 | 82.4 ± 7.7 | 141.4 ± 8.3 | 81.6 ± 11.7 |
| **Week 2, *n*** | 52 | 52 | 16 | 16 | 36 | 36 |
| Mean ± SD | 133.8 ± 10.0 | 79.5 ± 10.5 | 130.9 ± 10.3 | 78.8 ± 6.7 | 135.0 ± 9.7 | 79.9 ± 11.8 |
| Change from baseline | −7.1 ± 8.2*** | −2.3 ± 5.0** | −9.3 ± 6.7*** | −3.7 ± 4.2** | −6.2 ± 8.7*** | −1.6 ± 5.2 |
| **Week 4, *n*** | 57 | 57 | 18 | 18 | 39 | 39 |
| Mean ± SD | 133.1 ± 10.1 | 78.8 ± 10.3 | 131.2 ± 11.4 | 78.6 ± 7.5 | 133.9 ± 9.5 | 78.9 ± 11.4 |
| Change from baseline | −8.0 ± 7.7*** | −3.1 ± 5.3*** | −9.1 ± 7.0*** | −3.8 ± 4.6** | −7.4 ± 8.1*** | −2.7 ± 5.7** |

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|---|---|---|---|---|---|---|
| **Week 6, *n*** | 56 | 56 | 18 | 18 | 38 | 38 |
| Mean ± SD | 129.6 ± 8.5 | 77.1 ± 9.2 | 128.5 ± 9.7 | 77.3 ± 7.5 | 130.1 ± 8.0 | 77.0 ± 10.0 |
| Change from baseline | −11.3 ± 7.3*** | −4.5 ± 5.0*** | −11.8 ± 7.5*** | −5.1 ± 5.5** | −11.1 ± 7.3*** | −4.3 ± 4.7*** |
| **Week 8, *n*** | 57 | 57 | 18 | 18 | 39 | 39 |
| Mean ± SD | 130.0 ± 9.7 | 77.2 ± 9.7 | 129.3 ± 12.0 | 77.4 ± 8.1 | 130.4 ± 8.6 | 77.1 ± 10.4 |
| Change from baseline | −11.0 ± 8.1*** | −4.7 ± 5.1*** | −11.1 ± 7.8*** | −5.0 ± 5.9** | −11.0 ± 8.4*** | −4.6 ± 4.7*** |
| **Week 10, *n*** | 55 | 55 | 17 | 17 | 38 | 38 |
| Mean ± SD | 129.8 ± 10.1 | 77.3 ± 10.3 | 129.4 ± 11.8 | 77.4 ± 8.8 | 130.0 ± 9.4 | 77.3 ± 11.0 |
| Change from baseline | −11.1 ± 8.7*** | −4.4 ± 6.5*** | −10.8 ± 6.8*** | −5.4 ± 5.7** | −11.2 ± 9.6*** | −3.9 ± 6.8** |
| **Week 12, *n*** | 55 | 55 | 17 | 17 | 38 | 38 |
| Mean ± SD | 130.0 ± 12.3 | 76.4 ± 10.5 | 129.2 ± 15.0 | 75.5 ± 10.2 | 130.4 ± 11.1 | 76.7 ± 10.7 |
| Change from baseline | −11.1 ± 9.8*** | −5.4 ± 7.1*** | −11.8 ± 9.2*** | −7.3 ± 7.5*** | −10.8 ± 10.1*** | −4.5 ± 6.8*** |
| **Week 24, *n*** | 55 | 55 | 17 | 17 | 38 | 38 |
| Mean ± SD | 129.1 ± 10.9 | 77.3 ± 10.6 | 125.8 ± 11.6 | 75.6 ± 9.3 | 130.5 ± 10.4 | 78.0 ± 11.2 |
| Change from baseline | −11.8 ± 10.5*** | −4.6 ± 6.7*** | −13.8 ± 9.1*** | −6.4 ± 6.7** | −11.0 ± 11.1*** | −3.8 ± 6.7** |
| **EOT, *n*** | 58 | 58 | 19 | 19 | 39 | 39 |
| Mean ± SD | 129.5 ± 11.7 | 77.4 ± 10.5 | 127.5 ± 14.2 | 76.3 ± 9.5 | 130.5 ± 10.3 | 77.9 ± 11.0 |
| Change from baseline | −11.5 ± 10.7*** | −4.5 ± 6.6*** | −12.6 ± 10.3*** | −6.1 ± 6.6*** | −10.9 ± 10.9*** | −3.7 ± 6.6** |
| **Office BP** | | | | | | |
| **Baseline, *n*** | 58 | 58 | 19 | 19 | 39 | 39 |
| Mean ± SD | 145.9 ± 14.3 | 85.3 ± 12.8 | 144.9 ± 12.7 | 85.4 ± 11.9 | 146.3 ± 15.1 | 85.2 ± 13.3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Week 4, *n*** | 57 | 57 | 18 | 18 | 39 | 39 |
| Mean ± SD | 137.4 ± 11.2 | 82.5 ± 12.2 | 139.2 ± 12.1 | 82.0 ± 10.4 | 136.6 ± 10.8 | 82.7 ± 13.1 |
| Change from baseline | −8.1 ± 16.5*** | −2.6 ± 9.3* | −4.5 ± 18.1 | −2.7 ± 9.8 | −9.8 ± 15.6*** | −2.5 ± 9.2 |
| **Week 8, *n*** | 33 | 33 | 9 | 9 | 24 | 24 |
| Mean ± SD | 135.7 ± 14.8 | 82.5 ± 10.6 | 138.6 ± 16.4 | 85.0 ± 10.6 | 134.6 ± 14.4 | 81.6 ± 10.7 |
| Change from baseline | −13.2 ± 15.1*** | −5.4 ± 9.9** | −7.4 ± 14.2 | −1.4 ± 10.8 | −15.4 ± 15.1*** | −6.8 ± 9.4** |
| **Week 12, *n*** | 56 | 56 | 18 | 18 | 38 | 38 |
| Mean ± SD | 131.9 ± 12.5 | 79.6 ± 10.9 | 126.9 ± 10.2 | 78.0 ± 10.2 | 134.2 ± 12.9 | 80.3 ± 11.3 |
| Change from baseline | −13.9 ± 14.2*** | −5.9 ± 9.5*** | −16.8 ± 11.1*** | −6.7 ± 9.2** | −12.5 ± 15.3*** | −5.6 ± 9.8** |
| **Week 24, *n*** | 52 | 52 | 15 | 15 | 37 | 37 |
| Mean ± SD | 130.8 ± 11.3 | 78.5 ± 11.6 | 126.9 ± 12.7 | 76.5 ± 12.4 | 132.3 ± 10.4 | 79.3 ± 11.3 |
| Change from baseline | −14.9 ± 15.0*** | −7.3 ± 9.0*** | −16.6 ± 15.6** | −7.5 ± 9.8* | −14.3 ± 15.0*** | −7.2 ± 8.8*** |
| **EOT, *n*** | 57 | 57 | 18 | 18 | 39 | 39 |
| Mean ± SD | 130.4 ± 10.9 | 78.5 ± 11.3 | 127.0 ± 11.6 | 77.8 ± 11.8 | 131.9 ± 10.3 | 78.8 ± 11.2 |
| Change from baseline | −15.1 ± 14.4*** | −6.5 ± 9.3*** | −16.7 ± 14.1*** | −6.9 ± 9.7** | −14.4 ± 14.7*** | −6.4 ± 9.3*** |

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs. baseline, paired *t*-test.

*BP* blood pressure, *CCB* calcium channel blocker, *DBP* diastolic blood pressure, *EOT* end of treatment, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure, *SD* standard deviation

**Table S4**. Change from baseline in BP (per protocol set)

| | Total *N* = 46 | | Subcohorts | | | |
|---|---|---|---|---|---|---|
| | | | RASi *n* = 15 | | CCB *n* =31 | |
| | SBP, mmHg | DBP, mmHg | SBP, mmHg | DBP, mmHg | SBP, mmHg | DBP, mmHg |
| **Morning home BP** | | | | | | |
| **Baseline, *n*** | 46 | 46 | 15 | 15 | 31 | 31 |
| Mean ± SD | 141.5 ± 8.0 | 84.6 ± 10.3 | 140.8 ± 7.9 | 85.2 ± 6.8 | 141.9 ± 8.1 | 84.3 ± 11.8 |
| **Week 2, *n*** | 42 | 42 | 13 | 13 | 29 | 29 |
| Mean ± SD | 134.2 ± 10.5 | 82.3 ± 10.6 | 134.2 ± 14.3 | 84.1 ± 9.7 | 134.2 ± 8.6 | 81.6 ± 11.0 |
| Change from baseline | −7.0 ± 8.9*** | −2.5 ± 4.9** | −6.3 ± 11.7 | −2.1 ± 5.7 | −7.3 ± 7.6*** | −2.7 ± 4.5** |
| **Week 4, *n*** | 45 | 45 | 14 | 14 | 31 | 31 |
| Mean ± SD | 134.1 ± 10.0 | 81.8 ± 10.5 | 134.3 ± 11.7 | 81.7 ± 8.3 | 134.0 ± 9.4 | 81.8 ± 11.5 |
| Change from baseline | −7.6 ± 8.2*** | −2.7 ± 4.5*** | −6.9 ± 7.9** | −3.4 ± 4.3* | −7.9 ± 8.5*** | −2.5 ± 4.6** |
| **Week 6, *n*** | 44 | 44 | 14 | 14 | 30 | 30 |
| Mean ± SD | 131.3 ± 9.7 | 80.6 ± 9.8 | 133.9 ± 12.8 | 82.7 ± 8.0 | 130.1 ± 7.9 | 79.7 ± 10.6 |
| Change from baseline | −10.0 ± 9.5*** | −3.6 ± 5.3*** | −7.3 ± 10.1* | −2.4 ± 5.4 | −11.2 ± 9.1*** | −4.1 ± 5.2*** |
| **Week 8, *n*** | 45 | 45 | 14 | 14 | 31 | 31 |
| Mean ± SD | 131.5 ± 9.9 | 80.5 ± 9.8 | 132.6 ± 14.0 | 81.1 ± 8.3 | 131.0 ± 7.7 | 80.3 ± 10.6 |
| Change from baseline | −10.2 ± 9.7*** | −4.0 ± 5.7*** | −8.6 ± 11.8* | −3.9 ± 6.1* | −10.9 ± 8.8*** | −4.0 ± 5.6*** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Week 10, *n*** | 44 | 44 | 14 | 14 | 30 | 30 |
| Mean ± SD | 130.3± 9.0 | 79.4 ± 8.9 | 131.4 ± 11.5 | 79.9 ± 7.4 | 129.7 ± 7.8 | 79.2 ± 9.6 |
| Change from baseline | −11.0 ± 9.1*** | −4.8 ± 5.1*** | −9.8 ± 8.2*** | −5.1 ± 5.1** | −11.6 ± 9.6*** | −4.6 ± 5.1*** |
| **Week 12, *n*** | 44 | 44 | 14 | 14 | 30 | 30 |
| Mean ± SD | 131.2 ± 11.7 | 79.6 ± 9.8 | 133.3 ± 14.2 | 79.9 ± 7.8 | 130.2 ± 10.5 | 79.4 ± 10.7 |
| Change from baseline | −10.1 ± 11.0*** | −4.6 ± 6.0*** | −7.9 ± 11.2* | −5.1 ± 7.7* | −11.1 ± 10.9*** | −4.4 ± 5.2*** |
| **Week 24, *n*** | 43 | 43 | 13 | 13 | 30 | 30 |
| Mean ± SD | 130.6 ± 11.2 | 80.3 ± 10.6 | 129.4 ± 13.5 | 79.2 ± 8.3 | 131.1 ± 10.3 | 80.7 ± 11.5 |
| Change from baseline | −11.0 ± 12.1*** | −4.6 ± 6.5*** | −11.2 ± 10.1** | −5.8 ± 5.8** | −10.9 ± 13.0*** | −4.0 ± 6.7** |
| **EOT, *n*** | 46 | 46 | 15 | 15 | 31 | 31 |
| Mean ± SD | 131.0 ± 12.3 | 80.4 ± 10.7 | 131.3 ± 16.1 | 80.7 ± 8.8 | 130.8 ± 10.2 | 80.3 ± 11.6 |
| Change from baseline | −10.5 ± 12.5*** | −4.2 ± 6.6*** | −9.5 ± 12.1** | −4.5 ± 6.8* | −11.0 ± 12.8*** | −4.0 ± 6.6** |
| **Bedtime home BP** | | | | | | |
| **Baseline, *n*** | 46 | 46 | 15 | 15 | 31 | 31 |
| Mean ± SD | 140.0 ± 7.8 | 81.6 ± 10.8 | 138.6 ± 8.7 | 82.3 ± 7.8 | 140.6 ± 7.4 | 81.3 ± 12.1 |
| **Week 2, *n*** | 42 | 42 | 13 | 13 | 29 | 29 |
| Mean ± SD | 132.9 ± 9.2 | 79.0 ± 10.2 | 129.8 ± 11.1 | 78.7 ± 6.9 | 134.3 ± 8.0 | 79.2 ± 11.5 |
| Change from baseline | −7.0 ± 7.0*** | −2.6 ± 4.4*** | −9.1 ± 6.9*** | −4.3 ± 4.4** | −6.1 ± 7.0*** | −1.8 ± 4.2* |
| **Week 4, *n*** | 45 | 45 | 14 | 14 | 31 | 31 |
| Mean ± SD | 132.4 ± 9.6 | 78.5 ± 10.4 | 128.9 ± 10.9 | 77.9 ± 8.0 | 133.9 ± 8.6 | 78.8 ± 11.4 |
| Change from baseline | −7.7 ± 7.6*** | −3.1 ± 4.8*** | −9.9 ± 6.8*** | −4.4 ± 4.3** | −6.7 ± 7.9*** | −2.5 ± 5.0* |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Week 6, *n*** | 44 | 44 | 14 | 14 | 30 | 30 |
| Mean ± SD | 129.1 ± 7.7 | 77.0 ± 9.3 | 127.7 ± 10.3 | 77.3 ± 7.6 | 129.8 ± 6.2 | 76.9 ± 10.1 |
| Change from baseline | −10.7 ± 7.7*** | −4.2 ± 5.1*** | −11.1 ± 8.1*** | −5.0 ± 6.1** | −10.6 ± 7.6*** | −3.8 ± 4.6*** |
| **Week 8, *n*** | 45 | 45 | 14 | 14 | 31 | 31 |
| Mean ± SD | 129.3 ± 9.1 | 77.1 ± 9.9 | 128.1 ± 13.2 | 77.6 ± 8.9 | 129.8 ± 6.7 | 76.9 ± 10.5 |
| Change from baseline | −10.8 ± 8.2*** | −4.5 ± 5.1*** | −10.7 ± 8.5*** | −4.6 ± 6.6* | −10.8 ± 8.2*** | −4.4 ± 4.4*** |
| **Week 10, *n*** | 44 | 44 | 14 | 14 | 30 | 30 |
| Mean ± SD | 129.0 ± 9.4 | 76.7 ± 9.9 | 128.6 ± 12.3 | 76.7 ± 9.2 | 129.2 ± 7.9 | 76.7 ± 10.3 |
| Change from baseline | −10.8 ± 8.6*** | −4.5 ± 5.8*** | −10.1 ± 7.0*** | −5.6 ± 6.2** | −11.1 ± 9.4*** | −4.0 ± 5.7*** |
| **Week 12, *n*** | 43 | 43 | 13 | 13 | 30 | 30 |
| Mean ± SD | 128.9 ± 11.7 | 75.6 ± 10.0 | 128.5 ± 16.1 | 75.2 ± 10.5 | 129.1 ± 9.5 | 75.7 ± 10.0 |
| Change from baseline | −11.2 ± 10.0*** | −5.8 ± 6.7*** | −10.9 ± 9.9** | −7.6 ± 8.4** | −11.3 ± 10.2*** | −5.1 ± 5.9*** |
| **Week 24, *n*** | 43 | 43 | 13 | 13 | 30 | 30 |
| Mean ± SD | 128.8 ± 10.4 | 77.3 ± 10.6 | 124.9 ± 12.0 | 75.8 ± 9.7 | 130.5 ± 9.3 | 78.0 ± 11.1 |
| Change from baseline | −11.0 ± 10.7*** | −4.2 ± 6.2*** | −12.8 ± 9.8*** | −5.9 ± 7.5* | −10.2 ± 11.2*** | −3.5 ± 5.5** |
| **EOT, *n*** | 46 | 46 | 15 | 15 | 31 | 31 |
| Mean ± SD | 129.4 ± 11.4 | 77.5 ± 10.5 | 127.1 ± 15.1 | 76.7 ± 9.8 | 130.5 ± 9.2 | 77.9 ± 11.0 |
| Change from baseline | −10.6 ± 10.9*** | −4.1 ± 6.1*** | −11.5 ± 11.0** | −5.5 ± 7.3* | −10.2 ± 11.0*** | −3.4 ± 5.5** |
| **Office BP** | | | | | | |
| **Baseline, *n*** | 46 | 46 | 15 | 15 | 31 | 31 |
| Mean ± SD | 145.6 ± 14.9 | 85.6 ± 12.9 | 146.1 ± 14.2 | 86.8 ± 12.5 | 145.3 ± 15.5 | 85.0± 13.3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Week 4, *n*** | 45 | 45 | 14 | 14 | 31 | 31 |
| Mean ± SD | 137.7 ± 10.4 | 82.9 ± 12.3 | 141.7 ± 11.4 | 84.7 ± 8.0 | 135.9 ± 9.6 | 82.1 ± 13.9 |
| Change from baseline | −7.4 ± 17.7** | −2.4 ± 9.5 | −2.8 ± 19.3 | −1.3 ± 9.8 | −9.4 ± 16.8** | −3.0 ± 9.5 |
| **Week 8, *n*** | 26 | 26 | 6 | 6 | 20 | 20 |
| Mean ± SD | 136.7 ± 14.4 | 83.7 ± 9.6 | 145.3 ± 16.3 | 89.8 ± 7.8 | 134.2 ± 13.2 | 81.9 ± 9.5 |
| Change from baseline | −12.9 ± 15.3*** | −5.1 ± 8.5** | −3.5 ± 16.2 | −1.5 ± 9.9 | −15.7 ±14.2*** | −6.2 ± 7.9** |
| **Week 12, *n*** | 44 | 44 | 14 | 14 | 30 | 30 |
| Mean ± SD | 130.5 ± 10.3 | 78.9 ± 10.5 | 127.0 ± 10.8 | 78.5 ± 11.1 | 132.1 ± 9.9 | 79.0 ± 10.4 |
| Change from baseline | −14.9 ± 14.0*** | −7.0 ± 8.9*** | −17.5 ± 11.6*** | −7.5 ± 10.0* | −13.7 ± 15.0*** | −6.8 ± 8.6*** |
| **Week 24, *n*** | 42 | 42 | 12 | 12 | 30 | 30 |
| Mean ± SD | 130.1 ± 8.8 | 77.8 ± 11.0 | 126.3 ± 9.3 | 76.2 ± 12.3 | 131.7 ± 8.2 | 78.4 ±10.5 |
| Change from baseline | −15.2 ± 14.2*** | −8.1 ± 7.9*** | −18.0 ± 12.8*** | −9.7 ± 7.8** | −14.1 ± 14.8*** | −7.4 ± 8.0*** |
| **EOT, *n*** | 45 | 45 | 14 | 14 | 31 | 31 |
| Mean ± SD | 129.9 ± 8.6 | 77.7 ± 10.8 | 126.6 ± 8.7 | 77.1 ± 11.7 | 131.4 ± 8.3 | 78.0 ± 10.6 |
| Change from baseline | −15.2 ± 13.8*** | −7.6 ± 8.2*** | −17.9 ± 11.8*** | −8.9 ± 8.4** | −13.9 ± 14.6*** | −7.0 ± 8.2*** |

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs. baseline, paired *t*-test.

*BP* blood pressure, *CCB* calcium channel blocker, *DBP* diastolic blood pressure, *EOT* end of treatment, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure, *SD* standard deviation

**Table S5.** Achievement rate of target BP levels at Week 24 (full analysis set)

| | | Subcohorts | |
|---|---|---|---|
| | **Total** | **RASi** | **CCB** |
| | ***N* = 58** | ***n* = 19** | ***n* = 39** |
| Morning home BP | | | |
| *n* (%) | 33 (56.9) | 12 (63.2) | 21 (53.8) |
| 95% CI | [43.2, 69.8] | [38.4, 83.7] | [37.2, 69.9] |
| Bedtime home BP | | | |
| *n* (%) | 35 (60.3) | 13 (68.4) | 22 (56.4) |
| 95% CI | [46.6, 73.0] | [43.4, 87.4] | [39.6, 72.2] |
| Office BP | | | |
| *n* (%) | 39 (67.2) | 12 (63.2) | 27 (69.2) |
| 95% CI | [53.7, 79.0] | [38.4, 83.7] | [52.4, 83.0] |

95% CIs were calculated using the Clopper-Pearson method. The achievement rate of target BP levels was defined as home SBP/DBP < 135/85 mmHg and office SBP/DBP < 140/90 mmHg in the sitting position at Week 24.

*BP* blood pressure, *CCB* calcium channel blocker, *CI* confidence interval, *DBP* diastolic blood pressure, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure

**Table S6.** Achievement rate of target BP levels at Week 24 (per protocol set)

| | | Subcohorts | |
|---|---|---|---|
| | **Total** | **RASi** | **CCB** |
| | ***N* = 46** | ***n* = 15** | ***n* = 31** |
| Morning home BP | | | |
| *n* (%) | 26 (56.5) | 9 (60.0) | 17 (54.8) |
| 95% CI | [41.1, 71.1] | [32.3, 83.7] | [36.0, 72.7] |
| Bedtime home BP | | | |
| *n* (%) | 28 (60.9) | 10 (66.7) | 18 (58.1) |
| 95% CI | [45.4, 74.9] | [38.4, 88.2] | [39.1, 75.5] |
| Office BP | | | |
| *n* (%) | 33 (71.7) | 10 (66.7) | 23 (74.2) |
| 95% CI | [56.5, 84.0] | [38.4, 88.2] | [55.4, 88.1] |

95% CIs were calculated using the Clopper-Pearson method. The achievement rate of target BP levels was defined as home SBP/DBP < 135/85 mmHg and office SBP/DBP < 140/90 mmHg in the sitting position at Week 24.

*BP* blood pressure, *CCB* calcium channel blocker, *CI* confidence interval, *DBP* diastolic blood pressure, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure

**Table S7.** Changes from baseline in LVM and LVMI (full analysis set)

| | | | | Subcohorts | | | |
|---|---|---|---|---|---|---|---|
| | | | Total | RASi | | CCB | |
| | | *N* | *N* = 58 | *n* | *n* = 19 | *n* | *n* = 39 |
| **LVM, g** | | | | | | | |
| **Baseline** | Mean ± SD | 56 | 197.4 ± 50.9 | 17 | 216.9 ± 47.8 | 39 | 188.9 ± 50.5 |
| **Week 12** | Mean ± SD | 56 | 182.4 ± 50.4 | 18 | 191.6 ± 50.3 | 38 | 178.0 ± 50.5 |
| | Change from baseline | 54 | −13.0 ± 27.0 | 16 | −19.3 ± 24.3 | 38 | −10.3 ± 27.9 |
| | 95% CI | | [−20.3, −5.6]*** | | [−32.3, −6.4]** | | [−19.5, −1.1]* |
| | Percentage change from baseline | 54 | −6.9 ± 15.5 | 16 | −8.8 ± 12.6 | 38 | −6.1 ± 16.7 |
| | 95% CI | | [−10,5, −3.2]*** | | [−14.4, −2.8]** | | [−10.8, −1.2]* |
| **Week 24** | Mean ± SD | 52 | 175.8 ± 44.3 | 15 | 190.4 ± 44.6 | 37 | 169.9 ± 43.4 |
| | Change from baseline | 50 | −17.5 ± 34.3 | 13 | −30.1 ± 28.1 | 37 | −13.1 ± 35.6 |
| | 95% CI | | [−27.3, −7.8]*** | | [−47.0, −13.1]** | | [−25.0, −1.2]* |
| | Percentage change from baseline | 50 | −9.4 ± 20.8 | 13 | −13.5 ± 14.7 | 37 | −7.9 ± 22.5 |
| | 95% CI | | [−14.2, −4.4]*** | | [−20.4, −6.1]** | | [−14.0, −1.5]* |
| **EOT** | Mean ± SD | 56 | 180.1 ± 48.1 | 18 | 192.5 ± 41.2 | 38 | 174.3 ± 50.5 |
| | Change from baseline | 54 | −16.9 ± 33.7 | 16 | −23.6 ± 28.7 | 38 | −14.0 ± 35.5 |
| | 95% CI | | [−26.1, −7.7]*** | | [−39.0, −8.3]** | | [−25.7, −2.4]* |
| | Percentage change from baseline | 54 | −8.9 ± 20.2 | 16 | −10.8 ± 15.1 | 38 | −8.1 ± 22.2 |
| | 95% CI | | [−13.3, −4.2]*** | | [−17.2, −3.8]** | | [−13.9, −1.8]* |

| **LVMI, g/m²** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Baseline** | Mean ± SD | 56 | 118.1 ± 29.1 | 17 | 127.9 ± 27.4 | 39 | 113.9 ± 29.1 |
| **Week 12** | Mean ± SD | 56 | 109.5 ± 28.3 | 18 | 113.2 ± 28.2 | 38 | 107.8 ± 28.6 |
| | Change from baseline | 54 | −7.6 ± 17.0 | 16 | −10.9 ± 14.6 | 38 | −6.2 ± 17.9 |
| | 95% CI | | [−12.3, −3.0]** | | [−18.6, −3.1]** | | [−12.1, −0.4]* |
| | Percentage change from baseline | 54 | −6.5 ± 15.5 | 16 | −8.2 ± 12.7 | 38 | −5.7 ± 16.7 |
| | 95% CI | | [−10.1, −2.7]** | | [−13.9, −2.2]* | | [−10.4, −0.8]* |
| **Week 24** | Mean ± SD | 52 | 106.3 ± 25.7 | 15 | 113.0 ± 23.6 | 37 | 103.6 ± 26.4 |
| | Change from baseline | 50 | −10.3 ± 20.9 | 13 | −17.8 ± 17.2 | 37 | −7.7 ± 21.6 |
| | 95% CI | | [−16.3, −4.4]** | | [−28.2, −7.4]** | | [−14.9, −0.5]* |
| | Percentage change from baseline | 50 | −9.1 ± 20.6 | 13 | −13.2 ± 14.5 | 37 | −7.6 ± 22.3 |
| | 95% CI | | [−13.8, −4.1]*** | | [−20.1, −5.8]** | | [−13.6, −1.2]* |
| **EOT** | Mean ± SD | 56 | 108.3 ± 27.3 | 18 | 113.7 ± 21.7 | 38 | 105.8 ± 29.5 |
| | Change from baseline | 54 | −9.9 ± 20.5 | 16 | −13.9 ± 17.6 | 38 | −8.2 ± 21.6 |
| | 95% CI | | [−15.5, −4.3]*** | | [−23.2, −4.5]** | | [−15.3, −1.1]* |
| | Percentage change from baseline | 54 | −8.5 ± 20.0 | 16 | −10.4 ± 15.0 | 38 | −7.7 ± 22.0 |
| | 95% CI | | [−13.0, −3.9]*** | | [−16.9, −3.5]** | | [−13.6, −1.5]* |

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs. baseline, paired *t*-test.

*CCB* calcium channel blocker, *CI* confidence interval, *EOT* end of treatment, *LVM* left ventricular mass, *LVMI* left ventricular mass index, *RASi* renin-angiotensin system inhibitor, *SD* standard deviation

**Table S8.** Changes from baseline in LVM and LVMI (per protocol set)

| | | | | Subcohorts | | | |
|---|---|---|---|---|---|---|---|
| | | | Total | | RASi | | CCB |
| | | *N* | *N* = 46 | *n* | *n* = 15 | *n* | *n* = 31 |
| **LVM, g** | | | | | | | |
| **Baseline** | Mean ± SD | 46 | 194.5 ± 44.9 | 15 | 220.2 ± 48.9 | 31 | 182.1 ± 37.8 |
| **Week 12** | Mean ± SD | 44 | 184.5 ± 42.2 | 14 | 207.9 ± 34.3 | 30 | 173.6 ± 41.6 |
| | Change from baseline | 44 | −11.2 ± 27.2 | 14 | −19.3 ± 24.9 | 30 | −7.4 ± 27.7 |
| | 95% CI | | [−19.5, −2.9]** | | [−33.7, −4.9]* | | [−17.8, 2.9] |
| | Percentage change from baseline | 44 | −5.9 ± 15.5 | 14 | −8.2 ± 12.0 | 30 | −4.9 ± 16.9 |
| | 95% CI | | [−9.9, −1.7]** | | [−14.0, −2.0]* | | [−10.3, 0.9] |
| **Week 24** | Mean ± SD | 42 | 178.2 ± 44.6 | 12 | 203.6 ± 39.1 | 30 | 168.0 ± 43.2 |
| | Change from baseline | 42 | −17.9 ± 36.7 | 12 | −30.1 ± 29.3 | 30 | −13.1 ± 38.6 |
| | 95% CI | | [−29.4, −6.5]** | | [−48.7, −11.4]** | | [−27.5, 1.3] |
| | Percentage change from baseline | 42 | −9.6 ± 22.4 | 12 | −13.1 ± 15.2 | 30 | −8.1 ± 24.8 |
| | 95% CI | | [−15.1, −3.7]** | | [−20.6, −4.9]** | | [−15.4, −0.2]* |
| **EOT** | Mean ± SD | 44 | 178.9 ± 43.7 | 14 | 202.2 ± 36.2 | 30 | 168.0 ± 43.2 |
| | Change from baseline | 44 | −16.8 ± 36.2 | 14 | −24.9 ± 30.1 | 30 | −13.1 ± 38.6 |
| | 95% CI | | [−27.9, −5.8]** | | [−42.2, −7.5]** | | [−27.5, 1.3] |
| | Percentage change from baseline | 44 | −9.0 ± 22.1 | 14 | −10.9 ± 15.7 | 30 | −8.1 ± 24.8 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | 95% CI | | [−14.4, −3.3]** | | [−18.1, −3.1]* | | [−15.4, −0.2]* |
| **LVMI, g/m²** | | | | | | | |
| **Baseline** | Mean ± SD | 46 | 115.1 ± 24.7 | 15 | 130.6 ± 27.8 | 31 | 107.6 ± 19.4 |
| **Week 12** | Mean ± SD | 44 | 109.8 ± 24.5 | 14 | 123.1 ± 20.2 | 30 | 103.6 ± 24.2 |
| | Change from baseline | 44 | −6.1 ± 16.8 | 14 | −10.7 ± 15.1 | 30 | −4.0 ± 17.4 |
| | 95% CI | | [−11.2, −1.0]* | | [−19.4, −2.0]* | | [−10.5, 2.5] |
| | Percentage change from baseline | 44 | −5.4 ± 15.5 | 14 | −7.5 ± 12.2 | 30 | −4.4 ± 16.9 |
| | 95% CI | | [−9.4, −1.2]* | | [−13.4, −1.1]* | | [−9.8, 1.4] |
| **Week 24** | Mean ± SD | 42 | 105.7 ± 25.0 | 12 | 119.4 ± 21.7 | 30 | 100.2 ± 24.4 |
| | Change from baseline | 42 | −10.3 ± 22.3 | 12 | −17.9 ± 17.9 | 30 | −7.3 ± 23.4 |
| | 95% CI | | [−17.3, −3.4]** | | [−29.3, −6.5]** | | [−16.0, 1.4] |
| | Percentage change from baseline | 42 | −9.2 ± 22.2 | 12 | −12.9 ± 15.1 | 30 | −7.7 ± 24.5 |
| | 95% CI | | [−14.7, −3.4]** | | [−20.4, −4.8]** | | [−14.9, 0.2] |
| **EOT** | Mean ± SD | 44 | 106.2 ± 24.6 | 14 | 119.1 ± 20.2 | 30 | 100.2 ± 24.4 |
| | Change from baseline | 44 | −9.6 ± 22.0 | 14 | −14.6 ± 18.6 | 30 | −7.3 ± 23.4 |
| | 95% CI | | [−16.3, −2.9]** | | [−25.3, −3.9]* | | [−16.0, 1.4] |
| | Percentage change from baseline | 44 | −8.6 ± 21.9 | 14 | −10.6 ± 15.7 | 30 | −7.7 ± 24.5 |
| | 95% CI | | [−14.0, −2.9]** | | [−17.8, −2.7]* | | [−14.9, 0.2] |

*$p < 0.05$, **$p < 0.01$ vs. baseline, paired *t*-test.

*CCB* calcium channel blocker, *CI* confidence interval, *EOT* end of treatment, *LVM* left ventricular mass, *LVMI* left ventricular mass index, *RASi* renin-angiotensin system inhibitor, *SD* standard deviation

**Table S9.** Changes from baseline in LVEF, LAVI, E/A, E/e', and TRV (full analysis set)

| | | | | Subcohorts | | | |
|---|---|---|---|---|---|---|---|
| | | | Total | RASi | | CCB | |
| | | *N* | *N* = 58 | *n* | *n* = 19 | *n* | *n* = 39 |
| LVEF, % | | | | | | | |
| Baseline | Mean ± SD | 54 | 62.8 ± 6.1 | 16 | 61.8 ± 6.1 | 38 | 63.3 ± 6.1 |
| EOT | Mean ± SD | 54 | 64.5 ± 5.3 | 17 | 65.3 ± 6.5 | 37 | 64.2 ± 4.8 |
| | Change from baseline | | 1.4 ± 5.8 | | 3.1 ± 5.0 | | 0.7 ± 6.0 |
| | 95% CI | 51 | [−0.2, 3.0] | 15 | [0.3, 5.8]* | 36 | [−1.3, 2.8] |
| LAVI, ml/m$^2$ | | | | | | | |
| Baseline | Mean ± SD | 53 | 41.9 ± 13.8 | 14 | 46.7 ± 19.2 | 39 | 40.2 ± 11.1 |
| EOT | Mean ± SD | 53 | 39.1 ± 13.9 | 15 | 44.9 ± 17.4 | 38 | 36.8 ± 11.7 |
| | Change from baseline | | −2.6 ± 9.5 | | −1.8 ± 9.6 | | −2.9 ± 9.6 |
| | 95% CI | 52 | [−5.2, 0.1] | 14 | [−7.3, 3.7] | 38 | [−6.0, 0.3] |
| E/A | | | | | | | |
| Baseline | Mean ± SD | 55 | 0.9 ± 0.4 | 17 | 1.0 ± 0.4 | 38 | 0.9 ± 0.3 |
| EOT | Mean ± SD | 55 | 0.8 ± 0.3 | 18 | 0.9 ± 0.4 | 37 | 0.8 ± 0.3 |
| | Change from baseline | | −0.1 ± 0.2 | | −0.1 ± 0.2 | | −0.1 ± 0.3 |
| | 95% CI | 53 | [−0.2, 0.0]* | 16 | [−0.2, 0.0]* | 37 | [−0.2, 0.0] |
| E/e' | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Baseline | Mean ± SD | 50 | 9.7 ± 3.2 | 14 | 10.2 ± 2.8 | 36 | 9.6 ± 3.4 |
| EOT | Mean ± SD | 56 | 9.3 ± 3.6 | 18 | 9.0 ± 2.5 | 38 | 9.4 ± 4.0 |
| | Change from baseline | | −0.9 ± 2.5 | | −0.8 ± 2.5 | | −0.9 ± 2.6 |
| Mean ± SD | 95% CI | 48 | [−1.6, −0.2]* | 13 | [−2.4, 0.7] | 35 | [−1.8, 0.0]* |
| TRV, m/s | | | | | | | |
| Baseline | Mean ± SD | 48 | 2.2 ± 0.4 | 15 | 2.1 ± 0.4 | 33 | 2.3 ± 0.3 |
| EOT | Mean ± SD | 51 | 2.2 ± 0.5 | 14 | 2.1 ± 0.4 | 37 | 2.2 ± 0.5 |
| | Change from baseline | | 0.0 ± 0.4 | | −0.0 ± 0.5 | | 0.0 ± 0.4 |
| | 95% CI | 45 | [−0.1, 0.1] | 13 | [−0.3, 0.3] | 32 | [−0.1, 0.1] |

*$p < 0.05$ vs. baseline, paired *t*-test.

*CCB* calcium channel blocker, *CI* confidence interval, *E/A* ratio between the E-wave velocity and A-wave velocity of the pulsed-wave Doppler mitral flow image, *E/e'* ratio between E-wave velocity and the average early diastolic velocity of the lateral and septum at the mitral annulus level, *EOT* end of treatment, *LAVI* left atrial volume index, *LVEF* left ventricular ejection fraction, *RASi* renin-angiotensin system inhibitor, *SD* standard deviation, *TRV* tricuspid regurgitation velocity

**Table S10.** Changes from baseline in LVEF, LAVI, E/A, E/e′, and TRV (per protocol set)

| | | | | Subcohorts | | | |
|---|---|---|---|---|---|---|---|
| | | | Total | RASi | | CCB | |
| | | *N* | *N* = 46 | *n* | *n* = 15 | *n* | *n* = 31 |
| LVEF, % | | | | | | | |
| Baseline | Mean ± SD | 44 | 63.0 ± 6.4 | 14 | 62.3 ± 6.2 | 30 | 63.3 ± 6.5 |
| EOT | Mean ± SD | 43 | 64.1 ± 5.6 | 14 | 65.9 ± 6.6 | 29 | 63.2 ±4.9 |
| | Change from baseline | 41 | 0.7 ± 5.7 | 13 | 3.0 ± 5.2 | 28 | −0.4 ± 5.7 |
| | 95% CI | | [−1.1, 2.5] | | [−0.2, 6.1] | | [−2.6, 1.9] |
| LAVI, ml/m$^2$ | | | | | | | |
| Baseline | Mean ± SD | 44 | 41.8 ± 14.4 | 13 | 46.3 ± 19.9 | 31 | 39.9 ± 11.2 |
| EOT | Mean ± SD | 44 | 38.7 ± 14.6 | 14 | 44.9 ± 18.1 | 30 | 35.9 ± 11.9 |
| | Change from baseline | 43 | −2.7 ± 10.2 | 13 | −1.5 ± 9.9 | 30 | −3.3 ± 10.4 |
| | 95% CI | | [−5.9, 0.4] | | [−7.4, 4.5] | | [−7.2, 0.6] |
| E/A | | | | | | | |
| Baseline | Mean ± SD | 45 | 1.0 ± 0.4 | 15 | 1.0 ± 0.4 | 30 | 0.9 ± 0.3 |
| EOT | Mean ± SD | 43 | 0.9 ± 0.3 | 14 | 0.9 ± 0.4 | 29 | 0.8 ± 0.3 |
| | Change from baseline | 43 | −0.1 ± 0.2 | 14 | −0.1 ± 0.2 | 29 | −0.1 ± 0.3 |
| | 95% CI | | [−0.2, 0.0]** | | [−0.2, 0.0] | | [−0.2, 0.0] |
| E/e′ | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Baseline | Mean ± SD | 40 | 9.4 ± 3.1 | 12 | 9.9 ± 2.8 | 28 | 9.2 ± 3.2 |
| EOT | Mean ± SD | 44 | 9.2 ± 3.8 | 14 | 9.4 ± 2.6 | 30 | 9.1 ± 4.2 |
| | Change from baseline | 38 | −0.8 ± 2.5 | 11 | −0.2 ± 2.1 | 27 | −1.1 ± 2.6 |
| | 95% CI | | [−1.6, 0.0]* | | [−1.5, 1.2] | | [−2.1, 0.0]* |
| TRV, m/s | | | | | | | |
| Baseline | Mean ± SD | 41 | 2.2 ± 0.3 | 14 | 2.2 ± 0.4 | 27 | 2.3 ± 0.3 |
| EOT | Mean ± SD | 43 | 2.2 ± 0.4 | 13 | 2.1 ± 0.4 | 30 | 2.3 ± 0.4 |
| | Change from baseline | 38 | −0.0 ± 0.4 | 12 | −0.1 ± 0.5 | 26 | 0.0 ± 0.4 |
| | 95% CI | | [−0.2, 0.1] | | [−0.4, 0.2] | | [−0.2, 0.2] |

*$p < 0.05$, **$p < 0.01$ vs. baseline, paired *t*-test.

*CCB* calcium channel blocker, *CI* confidence interval, *E/A* ratio between the E-wave velocity and A-wave velocity of the pulsed-wave Doppler mitral flow image, *E/e'* ratio between E-wave velocity and the average early diastolic velocity of the lateral and septum at the mitral annulus level, *EOT* end of treatment, *LAVI* left atrial volume index, *LVEF* left ventricular ejection fraction, *RASi* renin-angiotensin system inhibitor, *SD* standard deviation, *TRV* tricuspid regurgitation velocity

**Table S11.** Changes in blood biomarker data from baseline (full analysis set)

| | | | | Subcohorts | | | |
|---|---|---|---|---|---|---|---|
| | | | Total | | RASi | | CCB |
| | | *N* | *N* = 58 | *n* | *n* = 19 | *n* | *n* = 39 |
| NT-proBNP, pg/ml | | | | | | | |
| Baseline | Mean ± SD | 58 | 191.8 ± 249.4 | 19 | 165.9 ± 154.8 | 39 | 204.5 ± 285.4 |
| Week 12 | Mean ± SD | 55 | 202.6 ± 363.1 | 18 | 141.8 ± 208.0 | 37 | 232.1 ± 417.8 |
| | Change from baseline | 55 | 9.7 ± 219.6 | 18 | −26.8 ± 116.7 | 37 | 27.5 ± 254.7 |
| | Percentage change from baseline | 55 | −15.9 ± 57.7 | 18 | −23.0 ± 60.5 | 37 | −12.2 ± 56.4 |
| | 95% CI | | [−25.6, −4.9]** | | [−39.1, −2.6]* | | [−24.4, 1.9] |
| Week 24 | Mean ± SD | 52 | 168.5 ± 259.5 | 15 | 142.2 ± 157.7 | 37 | 179.2 ± 292.1 |
| | Change from baseline | 52 | −7.8 ± 134.5 | 15 | −18.0 ± 101.2 | 37 | −3.6 ± 147.0 |
| | Percentage change from baseline | 52 | −13.9 ± 67.8 | 15 | −9.3 ± 100.0 | 37 | −15.7 ± 54.9 |
| | 95% CI | | [−25.5, −0.6]* | | [−38.2, 33.1] | | [−27.1, −2.5]* |
| EOT | Mean ± SD | 56 | 175.6 ± 258.8 | 18 | 141.2 ± 144.3 | 38 | 191.9 ± 298.6 |
| | Change from baseline | 56 | −14.1 ± 132.3 | 18 | −27.5 ± 95.8 | 38 | −7.7 ± 147.1 |
| | Percentage change from baseline | 56 | −15.4 ± 65.7 | 18 | −14.4 ± 91.0 | 38 | −15.8 ± 54.0 |
| | 95% CI | | [−26.1, −3.1]* | | [−37.9, 18.1] | | [−26.9, −3.0]* |
| PAC, pg/ml | | | | | | | |
| Baseline | Mean ± SD | 58 | 37.6 ± 22.6 | 19 | 24.5 ± 9.1 | 39 | 44.0 ± 24.4 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Week 12 | Mean ± SD | 55 | 77.7 ± 63.5 | 18 | 47.4 ± 49.9 | 37 | 92.5 ± 64.7 |
| | Change from baseline | 55 | 40.7 ± 47.2*** | 18 | 23.3 ± 45.8* | 37 | 49.2 ± 46.1*** |
| Week 24 | Mean ± SD | 52 | 78.6 ± 60.0 | 15 | 62.0 ± 79.9 | 37 | 85.4 ± 49.6 |
| | Change from baseline | 52 | 42.0 ± 52.9*** | 15 | 38.0 ± 76.0 | 37 | 43.7 ± 41.3*** |
| EOT | Mean ± SD | 56 | 77.7 ± 59.8 | 18 | 57.8 ± 74.1 | 38 | 87.1 ± 50.1 |
| | Change from baseline | 56 | 40.7 ± 51.6*** | 18 | 33.7 ± 70.1 | 38 | 44.0 ± 40.7*** |
| PRA, ng/ml/h | | | | | | | |
| Baseline | Mean ± SD | 58 | 1.3 ± 1.3 | 19 | 1.7 ± 1.7 | 39 | 1.1 ± 1.0 |
| Week 12 | Mean ± SD | 54 | 3.4 ± 4.7 | 18 | 5.5 ± 7.2 | 36 | 2.3 ± 2.3 |
| | Change from baseline | 54 | 2.1 ± 3.8*** | 18 | 3.9 ± 5.9* | 36 | 1.2 ± 1.5*** |
| Week 24 | Mean ± SD | 52 | 3.1 ± 5.6 | 15 | 6.0 ± 9.7 | 37 | 1.9 ± 1.5 |
| | Change from baseline | 52 | 1.9 ± 5.2* | 15 | 4.6 ± 9.3 | 37 | 0.8 ± 1.0*** |
| EOT | Mean ± SD | 56 | 3.5 ± 6.1 | 18 | 6.6 ± 10.0 | 38 | 2.0 ± 1.5 |
| | Change from baseline | 56 | 2.2 ± 5.6** | 18 | 5.1 ± 9.4* | 38 | 0.9 ± 1.0*** |

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs. baseline, paired *t*-test.

*CCB* calcium channel blocker, *CI* confidence interval, *EOT* end of treatment, *NT-proBNP* N-terminal pro-brain natriuretic peptide, *PAC* plasma aldosterone concentration, *PRA* plasma renin activity, *RASi* renin-angiotensin system inhibitor, *SD* standard deviation

**Table S12.** Changes in blood biomarker data from baseline (per protocol set)

| | | | | Subcohorts | | | |
|---|---|---|---|---|---|---|---|
| | | | Total | | RASi | | CCB |
| | | *N* | *N* = 46 | *n* | *n* = 15 | *n* | *n* = 31 |
| NT-proBNP, pg/ml | | | | | | | |
| Baseline | Mean ± SD | 46 | 148.4 ± 180.2 | 15 | 182.2 ± 158.8 | 31 | 132.1 ± 190.0 |
| Week 12 | Mean ± SD | 44 | 131.8 ± 212.4 | 14 | 158.3 ± 232.1 | 30 | 119.4 ± 205.4 |
| | Change from baseline | 44 | −11.9 ± 109.5 | 14 | −28.6 ± 128.8 | 30 | −4.1 ± 100.7 |
| | Percentage change from baseline | 44 | −20.0 ± 54.3 | 14 | −29.8 ± 57.7 | 30 | −15.0 ± 51.7 |
| | 95% CI | | [−29.9, −8.8]** | | [−46.1, −8.7]* | | [−27.3, −0.7]* |
| Week 24 | Mean ± SD | 42 | 148.6 ± 248.1 | 12 | 164.8 ± 168.9 | 30 | 142.2 ± 275.7 |
| | Change from baseline | 42 | 5.8 ± 134.6 | 12 | −26.5 ± 112.3 | 30 | 18.6 ± 142.2 |
| | Percentage change from baseline | 42 | −14.5 ± 70.7 | 12 | −18.2 ± 107.7 | 30 | −13.0 ± 56.4 |
| | 95% CI | | [−27.6, 1.0] | | [−48.6, 30.2] | | [−26.4, 2.8] |
| EOT | Mean ± SD | 44 | 147.0 ± 242.5 | 14 | 157.2 ± 157.1 | 30 | 142.2 ± 275.7 |
| | Change from baseline | 44 | 3.3 ± 132.0 | 14 | −29.7 ± 103.8 | 30 | 18.6 ± 142.2 |
| | Percentage change from baseline | 44 | −15.5 ± 69.3 | 14 | −20.5 ± 97.7 | 30 | −13.0 ± 56.4 |
| | 95% CI | | [−28.0, −0.8]* | | [−46.4, 17.8] | | [−26.4, 2.8] |
| PAC, pg/ml | | | | | | | |
| Baseline | Mean ± SD | 46 | 36.7 ± 22.8 | 15 | 22.6 ± 8.2 | 31 | 43.4 ± 24.6 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Week 12 | Mean ± SD | 44 | 76.3 ± 63.4 | 14 | 36.2 ± 29.6 | 30 | 95.0 ± 66.5 |
| | Change from baseline | 44 | 40.4 ± 45.5*** | 14 | 14.2 ± 27.9 | 30 | 52.7 ± 47.2*** |
| Week 24 | Mean ± SD | 42 | 74.8 ± 46.4 | 12 | 45.5 ± 34.9 | 30 | 86.5 ± 45.7 |
| | Change from baseline | 42 | 38.0 ± 36.6*** | 12 | 22.7 ± 33.1* | 30 | 44.2 ± 36.7*** |
| EOT | Mean ± SD | 44 | 72.2 ± 46.9 | 14 | 41.5 ± 33.7 | 30 | 86.5 ± 45.7 |
| | Change from baseline | 44 | 36.3 ± 36.6*** | 14 | 19.5 ± 31.5* | 30 | 44.2 ± 36.7*** |
| PRA, ng/ml/h | | | | | | | |
| Baseline | Mean ± SD | 46 | 1.2 ± 1.2 | 15 | 1.4 ± 1.5 | 31 | 1.1 ± 1.1 |
| Week 12 | Mean ± SD | 43 | 2.8 ± 3.1 | 14 | 3.7 ± 4.2 | 29 | 2.3 ± 2.4 |
| | Change from baseline | 43 | 1.6 ± 2.2*** | 14 | 2.5 ± 3.1** | 29 | 1.2 ± 1.6*** |
| Week 24 | Mean ± SD | 42 | 3.2 ± 6.0 | 12 | 6.3 ± 10.7 | 30 | 2.0 ± 1.5 |
| | Change from baseline | 42 | 2.1 ± 5.7* | 12 | 5.1 ± 10.3 | 30 | 0.9 ± 1.0*** |
| EOT | Mean ± SD | 44 | 3.2 ± 5.9 | 14 | 5.7 ± 9.9 | 30 | 2.0 ± 1.5 |
| | Change from baseline | 44 | 2.0 ± 5.6* | 14 | 4.5 ± 9.6 | 30 | 0.9 ± 1.0*** |

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs. baseline, paired *t*-test.

*CCB* calcium channel blocker, *CI* confidence interval, *EOT* end of treatment, *NT-proBNP* N-terminal pro-brain natriuretic peptide, *PAC* plasma aldosterone concentration, *PRA* plasma renin activity, *RASi* renin-angiotensin system inhibitor, *SD* standard deviation

**Table S13.** Incidences of serum potassium level ≥ 5.5 and ≥ 6.0 mEq/l (safety analysis set)

| | | Subcohorts | |
|---|---|---|---|
| | **Total** | **RASi** | **CCB** |
| | ***N* = 60** | ***n* = 21** | ***n* = 39** |
| Serum potassium ≥ 5.5 mEq/l | 3 (5.0) | 1 (4.8) | 2 (5.1) |
| Serum potassium ≥ 6.0 mEq/l | 0 (0.0) | 0 (0.0) | 0 (0.0) |

Data are *n* (%).

*CCB* calcium channel blocker, *RASi* renin-angiotensin system inhibitor

## Supplementary Figures

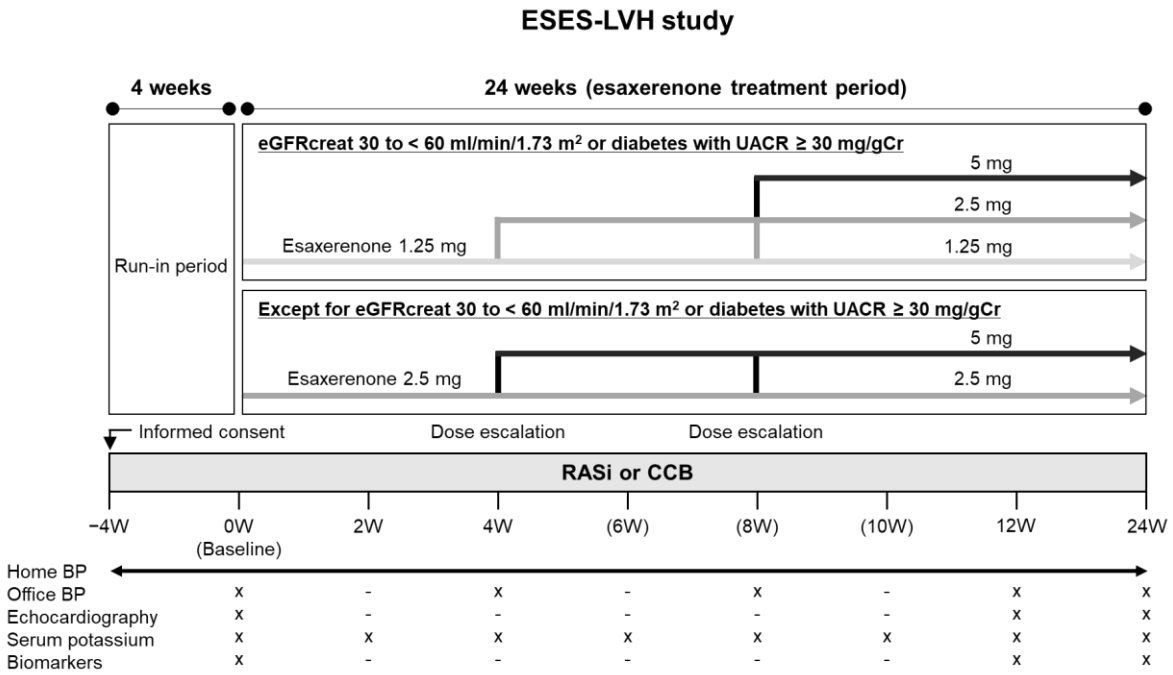


**Fig. S1** Study design

*BP* blood pressure, *CCB* calcium channel blocker, *eGFRcreat* creatinine-based estimated glomerular filtration rate, *RASi* renin-angiotensin system inhibitor, *UACR* urine albumin-creatinine ratio, *W* weeks

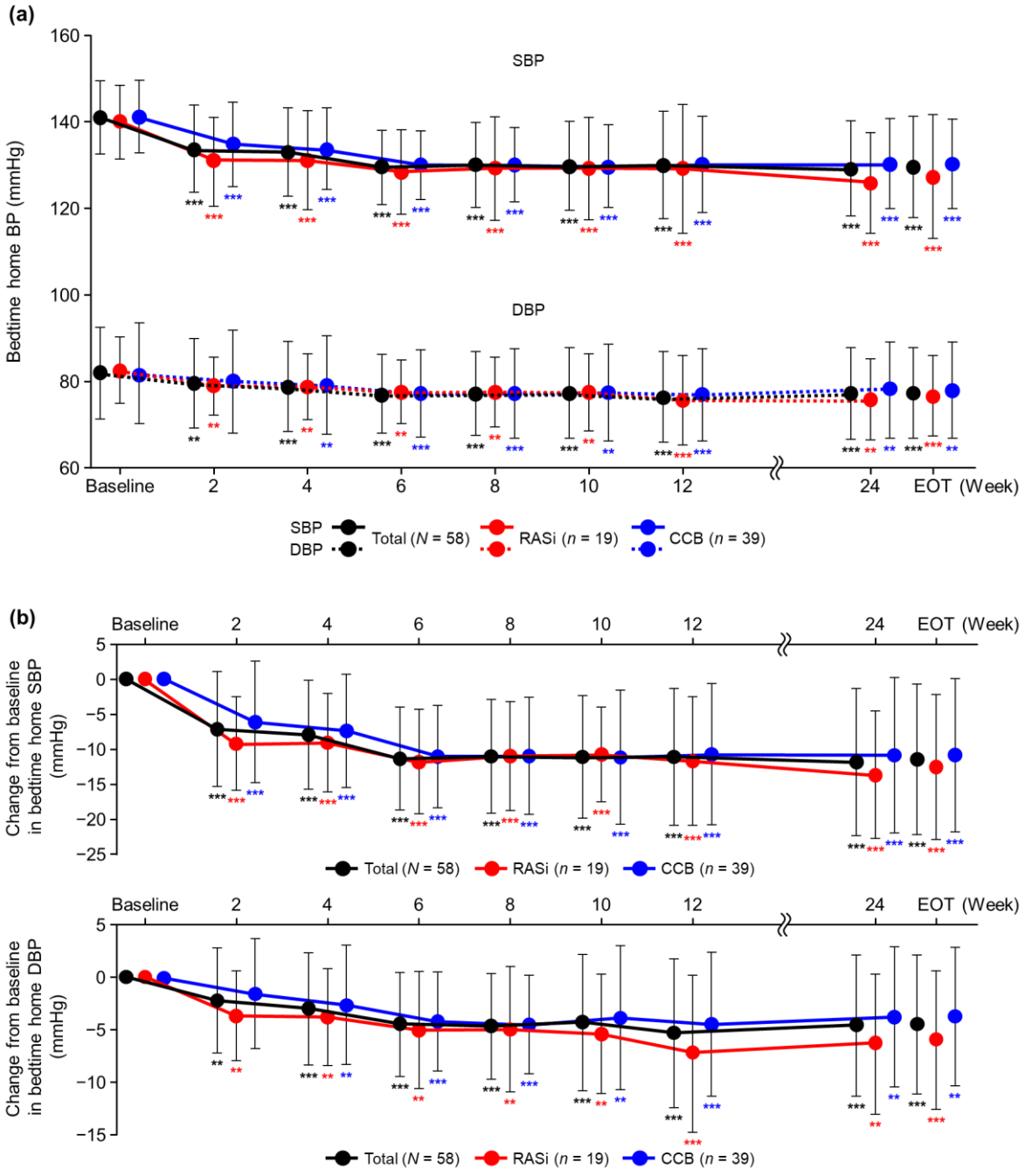


**Fig. S2** Time course changes (**a**) and changes from baseline (**b**) in bedtime home BP throughout the study period in the total population and RASi and CCB subcohorts (full analysis set).

Data are mean ± standard deviations.

**$p < 0.01$, ***$p < 0.001$ vs. baseline, paired *t*-test.

*BP* blood pressure, *CCB* calcium channel blocker, *DBP* diastolic blood pressure, *EOT* end of treatment, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure

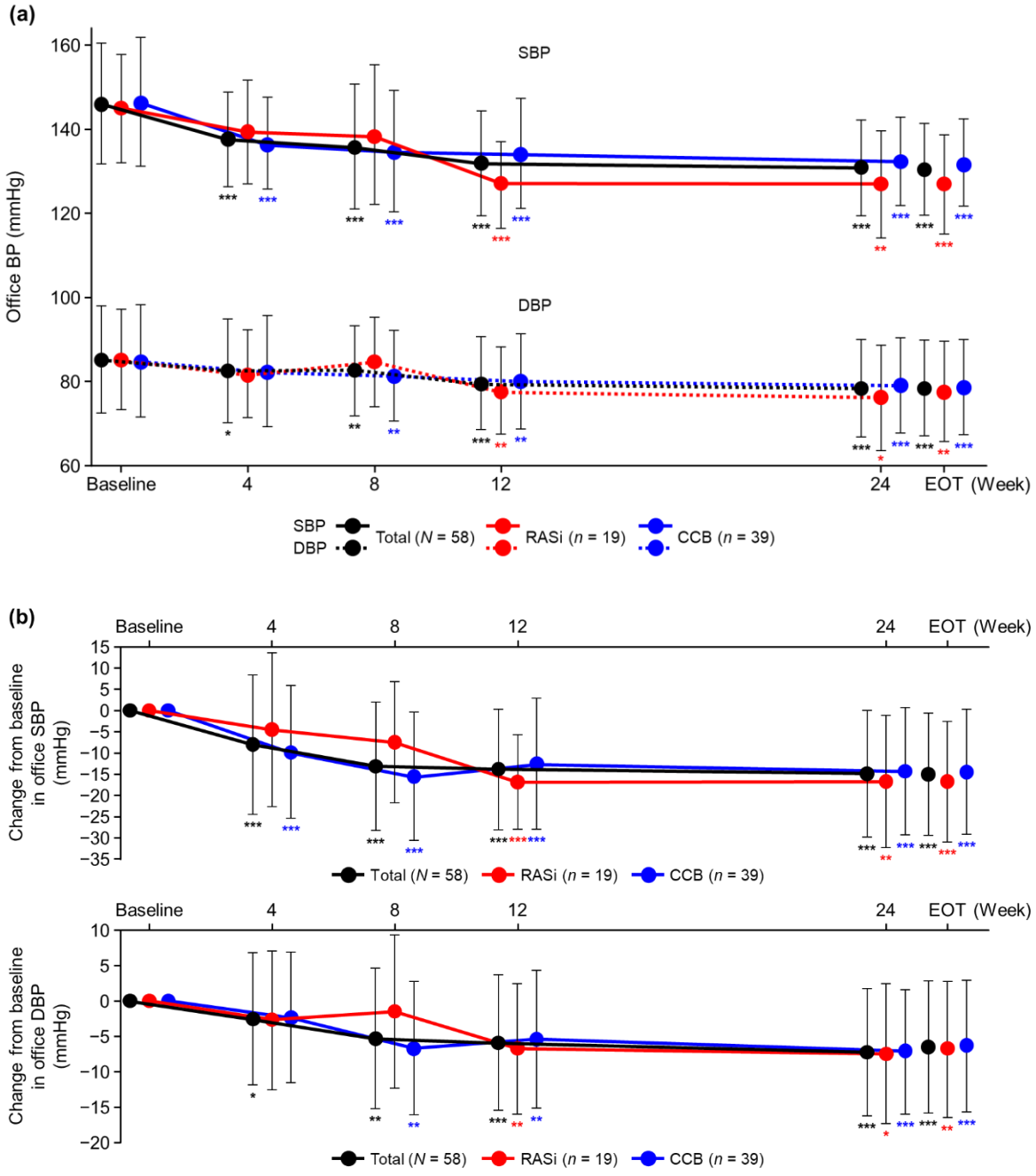


**Fig. S3** Time course changes (**a**) and changes from baseline (**b**) in office BP throughout the study period in the total population and RASi and CCB subcohorts (full analysis set). Data are mean ± standard deviations.

*$p$ < 0.05, **$p$ < 0.01, ***$p$ < 0.001 vs. baseline, paired $t$-test.

*BP* blood pressure, *CCB* calcium channel blocker, *DBP* diastolic blood pressure, *EOT* end of treatment, *RASi* renin-angiotensin system inhibitor, *SBP* systolic blood pressure

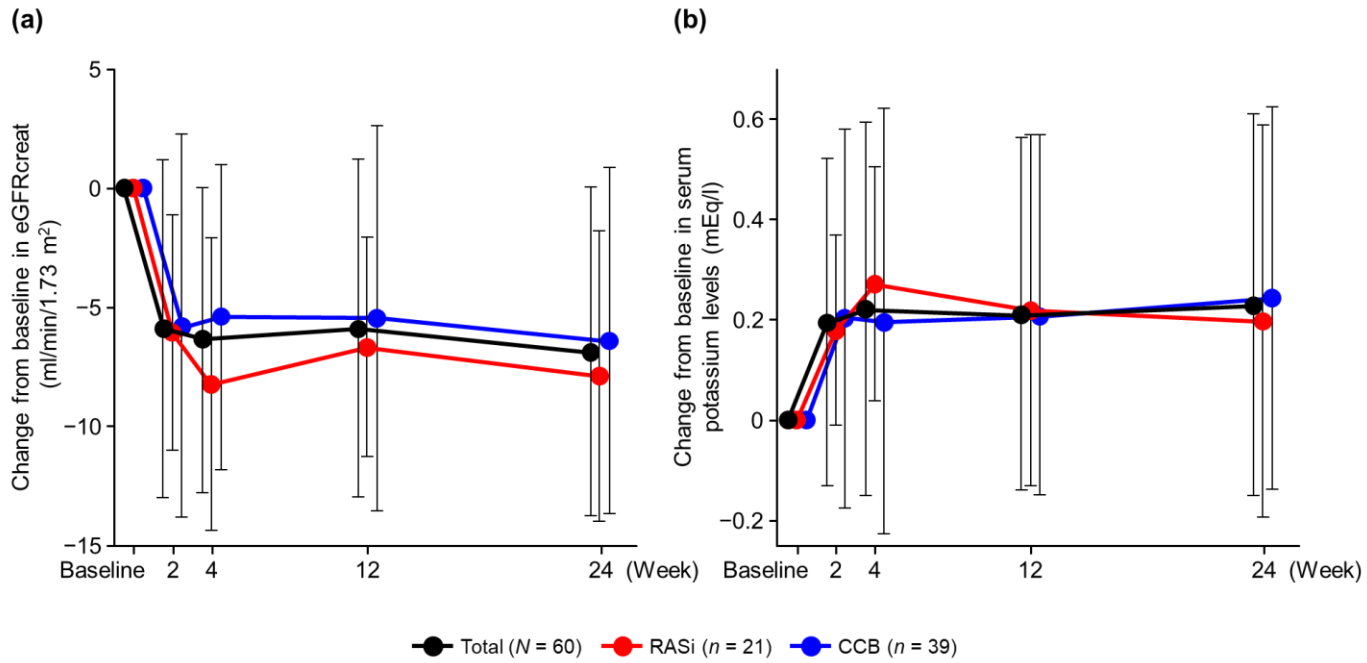


**Fig. S4** Time course changes from baseline in eGFRcreat (**a**) and serum potassium levels (**b**) throughout the study period in the total population and RASi and CCB subcohorts (safety analysis set).

Data are mean ± standard deviations.

*CCB* calcium channel blocker, *eGFRcreat* creatinine-based estimated glomerular filtration rate, *RASi* renin-angiotensin system inhibitor