**Supplemental APPENDIX**

**Supplemental Table 1**

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| **Parameters** | **Pre-discharge initiation*****N*=493** | **Post-discharge initiation*****N*=489** | **Total population*****N*=982** |
| Mean duration of index hospitalization stay, days, (SD) | 9.7 (4.8) | 8.5 (4.9) | 9.1 (4.9) |
| Mean time from admission to randomization, days (SD) | 7.3 (3.9) | 7.0 (4.1) | 7.1 (4.0) |
| Mean time from randomization to first dose, days (SD) | 0.6 (1.0) | 4.9 (4.7) | 2.7 (4.0) |
| Mean time from randomization to discharge, days (SD) | 2.4 (2.7) | 1.5 (2.1) | 2.0 (2.5) |
| Post-discharge group: Mean time from discharge to first dose, days (SD) | NA | 3.3 (4.4) | NA |

**Timing of initiation of sacubitril/valsartan and length of index hospitalization.** NA, not applicable to Pre-discharge initiation group. Number of days in hospital calculated as Date of discharge – Date of admission.

**Supplemental Table 2**

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| **Predictor** | **Discharge** | **4 Weeks** | **10 Weeks** |
|  | **p–value** | **p–value** | **p–value** |
| Age groups <65, ≥65 and <75, ≥75 | 0.7913, 0.9275 | 0.0012, 0.0083 (confounded) | 0.0004, 0.0390 (confounded) |
| eGFR at baseline | 0.3745 | <0.0001 | <0.0001 |
| Higher serum creatinine at baseline\*, Δ of 20 µmol/L | 0.4949 | <0.0001 | <0.0001 |
| No β-blocker before admission  | 0.7287 | 0.0002 | <0.0001 |
| No MRA before admission  | 0.4134 | <0.0001 | <0.0001 |
| No diuretics before admission  | 0.8584 | <0.0001 | <0.0001 |
| Hs-TnT at baseline\* | 0.4366 | 0.4269 | 0.2905 |
| *De novo* HF | 0.2863 | <0.0001 | <0.0001 |
| NYHA Class at randomization (I, II) vs (III, IV) | 0.9644 | 0.5044 | 0.2960 |
| Non-ischemic etiology | 0.8903 | <0.0001 | <0.0001 |
| Previous HF hospitalization within 12 months   | 0.3437 | <0.0001 | <0.0001 |
| EF (%) at baseline | 0.5717 | 0.0459 | 0.0427 |
| ***Medical histor*y** |
| No hypertension at baseline | 0.0007 | 0.0126 | 0.0047 |
| No AF at baseline | 0.9481 |  <0.0001 | 0.0004 |
| No prior MI | 0.5028 |  <0.0001 | <0.0001 |
| History of implantable device (CRT or ICD) | 0.1011 | 0.0096 | 0.0041 |
| ***Demographic characteristics at baseline*** |
| Weight group | 0.3140 | 0.9247 | 0.0570 |
| BMI (kg/m2) | 0.2579 (confounded) | 0.2290 | 0.0953 (confounded) |
| SBP  | 0.1599 | 0.6654 | 0.3694 |
| Number of days between index hospital admission to first dose of sacubitril/valsartan | 0.0938 | 0.9112 | 0.9551 |
| Duration of index hospitalization in days† | 0.8463 | 0.5304 | 0.7257 |
| Starting sacubitril/valsartan dose ≥49/51 mg b.i.d | 0.4619 | 0.1919 |  0.1421 |
| Accumulative dose | 0.1264 | 0.0174(confounded) | <0.0001 |
|  Higher NT-proBNP at baseline\*, Δ of 1000 pg/mL | Always included | Always included | Always included |
| ACEi/ARB naïve | 0.0676 | <0.0001 | <0.0001 |

**Predictors included in the univariate analysis**. Candidate predictors were identified from baseline and medical history variables and filtered in a univariate analysis at a level of p<0.2. In the final multivariate analysis models, only predictors with p<0.05, baseline NT-proBNP level and treatment group (for 4 and 10 Weeks) were maintained. \*Baseline assessment taken at randomization visit. †Time between index hospital admission and discharge visit 102: The duration of total hospital admission is usually reflecting: a) the severity of ADHF event b) severity of concomitant diseases and c) inability to discharge patient promptly due to administrative reasons (no caregivers at home or no free place in rehabilitation or long-term-care centers). ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; bpm, beats per minute; CRT, cardiac resynchronization therapy; CV, cardiovascular; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HF, heart failure; hs-TnT, high-sensitivity troponin T; ICD, implantable cardioverter defibrillator; IQR, interquartile range; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure.

**Supplemental Table 3**

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| **Predictor** | **Odds ratio** | **95% CI** | **p value** |
| Higher NT-proBNP at baseline\*, Δ of 1000 pg/mL | 1.050  | (0.995–1.109) | 0.0769 |
| ACEi/ARB naïve  | 1.298 | (0.825–2.042) | 0.2585 |
| Hypertension  | 2.065  | (1.260–3.382) | 0.0040 |
| Days from index hospitalization to first dose of sacubitril/valsartan | 0.949 | (0.901–1.000) | 0.0482 |

**Pre-discharge group multivariate predictor analyses to attain a favorable response (values of NT-proBNP either ≤1000 pg/mL or >30% reduction from baseline) at Discharge**. Multivariate logistic regression was used for the analyses and only predictors with p<0.05 were kept in the final model but higher NT-proBNP at baseline, Δ of 1000 pg/mL and ACEi/ARB stratification were both included as a covariate in the model regardless of the p-value. \* Baseline assessment taken at randomization visit. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; NT-proBNP, N-terminal pro-B-type natriuretic peptide. Safety set patients.

**Supplemental Table 4**

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| --- | --- | --- | --- |
| **Predictor** | **Odds ratio** | **95% CI** | **p value** |
| Treatment group pre-discharge vs. post-discharge | 1.196  | (0.899–1.591) | 0.2193 |
| Higher NT-proBNP at baseline\*, Δ of 1000 pg/mL | 1.175  | (1.116–1.236) | <0.0001 |
| Higher serum creatinine at baseline\*, Δ of 20 µmol/L | 0.834  | (0.751–0.928) | 0.0008 |
| *De novo* HF | 1.548  | (1.077–2.226) | 0.0182 |
| No AF at baseline  | 1.696  | (1.267–2.269) | 0.0004 |
| Starting sacubitril/valsartan dose ≥49/51 mg b.i.d | 1.550  | (1.025–2.344) | 0.0379 |
| ACEi/ARB naïve  | 1.582  | (1.130–2.213) | 0.0075 |
| No prior MI | 1.617  | (1.169–2.235) | 0.0036 |

**Multivariate predictor analyses to attain a favorable response (values of NT-proBNP either ≤1000 pg/mL, or with >30% reduction from baseline) at Week 4.** Only predictors with p<0.05 were kept in the final model but treatment group and higher NT-proBNP at baseline, Δ of 1000 pg/mL were included as covariates in the model regardless of the p-value. \* Baseline assessment taken at Randomization visit ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; HF, heart failure; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide. Safety set patients.

**Supplemental Table 5**

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| **Predictor** | **Odds ratio** | **95% CI** | **p value** |
| Treatment group pre-discharge vs. post-discharge | 1.034  | (0.767–1.393) | 0.8278 |
| Higher NT-proBNP at baseline\*, Δ of 1000 pg/mL | 1.204  | (1.134–1.277) | <0.0001 |
| Higher serum creatinine at baseline\*, Δ of 20 µmol/L | 0.822 | (0.737–0.917) | 0.0004 |
| *De novo* HF | 1.600  | (1.075–2.382) | 0.0206 |
| No AF at baseline | 1.384  | (1.022–1.873) | 0.0356 |
| Starting sacubitril/valsartan dose ≥49/51 mg b.i.d | 1.661  | (1.075–2.566) | 0.0222 |
| ACEi/ARB naïve | 1.698 | (1.193–2.418) | 0.0033 |
| No MRA before admission | 1.831  | (1.302–2.575) | 0.0005 |
| Non-ischemic etiology | 1.708  | (1.244–2.344) | 0.0009 |
| Weight group ≥100 kg | 1.571  | (1.082–2.282) | 0.0176 |

**Multivariate predictor analyses to attain a favorable response (values of NT-proBNP either ≤1000 pg/mL, or with >30% reduction from baseline) at Week 10.** Only predictors with p<0.05 were kept in the final model but treatment group and higher NT-proBNP at baseline, Δ of 1000 pg/mL were included as covariates in the model regardless of the p-value. \* Baseline assessment taken at Randomization visit; ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; HF, heart failure; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide. Safety set patients.

**Supplemental Figure 1**

**Kaplan-Meier plot of time from discharge to first HF rehospitalization or CV death by baseline NT-proBNP level through 26 weeks.** The p value was obtained from cox proportional hazards regression analysis model with median based subgroup, treatment initiation group. Baseline (at randomization) NT-proBNP, median from total n=991 study population was 1743 pg/mL. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; HF, heart failure; HR, hazard ratio; NT-proBNP, N-terminal-pro-B-type natriuretic peptide.



**Supplemental Figure 2**

**Kaplan-Meier plot of time from discharge to first HF rehospitalization or CV death by pre-discharge or post-discharge treatment initiation group.** The p value was obtained from cox proportional hazards regression analysis model by treatment initiation group. CV, cardiovascular; HF, heart failure; HR, hazard ratio

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