Examining the Short-Term Impact of Different Treatment Approaches on Clinical Outcomes in High-Acuity Heart Failure Patients: Methodologic Lessons from the AT HOME-HF Pilot Study

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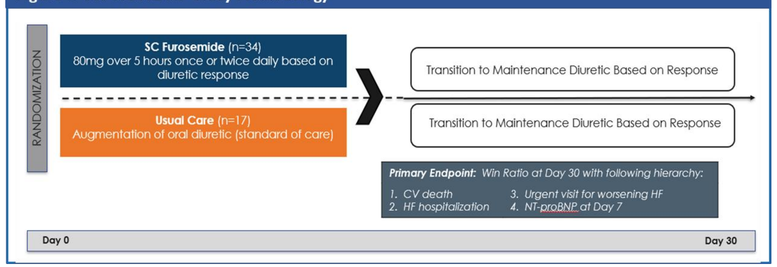
INTRODUCTION AND OBJECTIVES

- As the heart failure (HF) population grows and incentives increase for managing worsening HF outside the hospital, home administration of parenteral loop diuretics is becoming an attractive option.
- AT HOME-HF was an open-label, randomized pilot study exploring short-term patient-reported outcomes and safety with subcutaneous (SC) furosemide in patients with worsening congestion, compared with enhanced oral medical therapy in the outpatient setting.
- A hierarchical composite endpoint was utilized consisting of sequential individual comparisons for 30-day cardiovascular (CV) mortality; HF events, and 7-day change from baseline in NT-proBNP.
- The present analysis is to explore the performance of various outcome endpoints over a short time frame, the purpose was to explore performance of different measures of HF hospitalization, comparing 2 treatment strategies over 30 days, in this limited population with worsening HF.

METHODS

Figure 1. AT HOME-HF Study Methodology



- **Inclusion Criteria:** NYHA Class II-IV HF with signs of volume overload and > 1 of the following in the preceding 30 days: dyspnea, fatigue, exercise intolerance
- **Exclusion Criteria:** eGFR < 20; HR > 110; IV loop diuretic within the prior 24 hrs; expected instability with outpatient treatment
- Patients were randomized (2:1) to receive Furoscix 80 mg (up to 7 doses, once or twice daily based on diuretic response) or Usual Care **(Figure 1)**.
- The primary endpoint was assessed at 30 days, using the Finkelstein-Schoenfeld (FS) method, along a hierarchy of 4 endpoint components **(Figure 1)**.
- We compared an analysis of time-to-first hospitalization vs. total hospitalizations in quantifying treatment effect across the 2 arms of the AT HOME-HF Pilot Study.

RESULTS

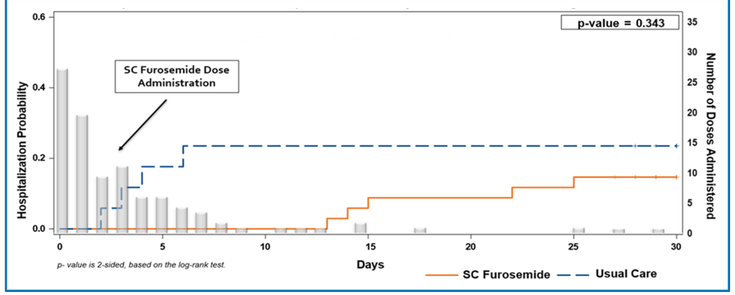
- 51 patients were randomized, 34 to Furoscix; 17 to Usual Care.
- Demographics and baseline characteristics are listed in **Table 1.**
- Mean (range) number of SC furosemide doses across the 30-day study period was 4 (1-9); 90% of doses were administered within first 7 days.

Table 1. Baseline Characteristics

Clinical Characteristic	SC Furosemide n=34	Usual Care n=17
Age, yrs (mean ± SD)*	63.5 ± 10.9	71.1 ± 11.0
Gender, Female n (%)	9 (26.5)	6 (35.3)
Body mass index, kg/m²	36 (7.9)	36.6 (9.9)
Race, n (%)		
Black or African American	11 (32.4)	4 (23.5)
White	23 (67.6)	13 (76.5)
NYHA Class, n (%)		
Class II	2 (5.9)	4 (23.5)
Class III	31 (91.2)	12 (70.6)
Class IV	1 (2.9)	1 (5.9)
NT-proBNP, pg/mL, median (min, max)**	1254.5 (5, 14,574)	3764.0 (460, 13,718)
Daily furosemide equivalent dose, mg, median (min, max)[b]	80 (40, 600)	80 (20, 400)
CKD, n (%)	13 (38.2)	6 (35.3)
eGFR, mL/min/1.73 m2 (mean ± SD)	55.0 (21.1)	48.9 (27.8)

*p < 0.05. [a]Mean (SD) 2249.4 (3208.0) and 5467.5 (4979.6) for Furoscix and Usual Care, respectively. [b]Mean (SD) 146.7 (141.7) and 124.7 (115.0) for Furoscix and Usual Care, respectively

Figure 2. Kaplan-Meir Estimate of HF Hospitalization at 30 days and SC Furosemide Timing



- For composite primary endpoint, win ratio was 1.11 (95% CI: 0.48 - 2.50; P = 0.806).
- Notable trends in changes from baseline favoring SC furosemide were observed for body weight, 6-minute walk distance, dyspnea scores, and Kansas City Cardiomyopathy Questionnaire (Konstam M, et al JACC HF 2024;12(11):1830-1841.

Table 2. Hospitalization Data

	SC Furosemide (n=34)	Usual Care (n=17)	RR/HR
HF Hospitalizations, n (%)	5 (14.7%)	4 (23.5%)	0.63[a] (0.19-2.03)[b]
Patients with > 1 Hospitalization	0	0	-
Days to Hospitalization	17.5	2.5	0.54[c] (0.14-2.00)[b]

(a) RR= rate ratio; (b) 95% CI; (c) HR= hazard ratio (neither statistically significant)

RESULTS, CONT.

- No patients in SC furosemide group were hospitalized for HF during first 7 days; all patients hospitalized for HF in usual care group were hospitalized during first 7 days.
- For patients hospitalized, median length of stay (LOS) was 10 days in SC furosemide group and 14.5 days in usual care group.
- A summary of individual endpoints and additional measures of hospitalization are summarized in **Table 3**.

Table 3. Individual Outcomes of Interest

	SC Furosemide (n=34)	Usual Care (n=17)	p-value
CV Death within 30 days	1 (2.9%)	0	
Difference, % (95% CI)	2.9 (-17.0, 15.9)		>0.999
HF Hospitalization within 30 days	5 (14.7%)	4 (23.5%)	
Difference, % (95% CI)	-8.8 (-36.4, 13.6)		0.459
Urgent ED/clinic visit for HF with IV diuretic administration or oral diuretic enhancement within 30 days, n	0	0	ND
NT-ProBNP at day 7 median change (IQR) pg/mL[a, b]	-7.2% (64.62)	-2.2 (48.82)	0.547
Median days to Hospitalization[c]	17.5	2.5	
HR, (95% CI)	0.54 (0.14, 2.0)		0.356
Median days HF Event-free Survival[d]	21.5	15.5	0.336

CV=Cardiovascular, IQR, interquartile range, HF=Heart Failure, CI=Confidence Interval, ND=Not determined
[a]In the SC furosemide group, 4 patients had a missing baseline or day 7 NT-proBNP value. In the Usual Care group, 6 patients had a missing baseline or day 7 NT-proBNP value. [b]In the SC furosemide group, 4 patients had a baseline NT-proBNP < 125 pg/mL and in the Usual Care group, 0 patients had a baseline NT-proBNP < 125 pg/mL. [c]Of patients with HF hospitalization (n=9). [d]HF related Hospitalization or Urgent ED/Clinic visit considered as Heart Failure Event. Out of 30 days, HF Event-free Survival was calculated for patients deceased or had HF Event occurred. Heart failure event-free (hospitalization for heart failure or Urgent ED/Clinic visits for heart failure) over 30 days are compared between treatment groups using the non-parametric Wilcoxon rank sum test.

SUMMARY AND CONCLUSIONS

- Within the AT HOME-HF pilot study, there were too few events to draw any firm between-group comparisons regarding HF hospitalization.
- Findings from this small study suggest that over a 30-day period, few patients will experience repeat HF hospitalization. However, timing of hospitalizations may be an important differentiating factor, suggesting that a time-to-first-event analysis is preferable to a total count of events.
- Larger scale clinical trials are needed to confirm these conclusions and explore options for more structured dosing recommendations, transition to oral agents, and outcome benefit of SC treatment.

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