ASM 2026
HFSA ANNUAL SCIENTIFIC MEETING
Where Heart Failure Teams Gather
October 9-12, 2026 | Phoenix, Arizona

Subcutaneous (SC) Injection of Furosemide: Consistent Pharmacokinetic and Pharmacodynamic Profiles Across Thigh And Arm Injection Sites Versus Intravenous Administration When Administered Via An Autoinjector

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INTRODUCTION

- During congestion oral furosemide absorption is variable, often requiring IV administration.
- Furoscix ReadyFlow (FUR SC) is a pH-neutral 80 mg/mL furosemide for SC self-administration by autoinjector in the outpatient setting.
- Prior studies showed bioequivalence (BE) to IV furosemide with comparable diuretic, natriuretic, and kaliuretic effects when given in the abdomen.
- Bioavailability (BA) at alternative subcutaneous sites remains unknown.

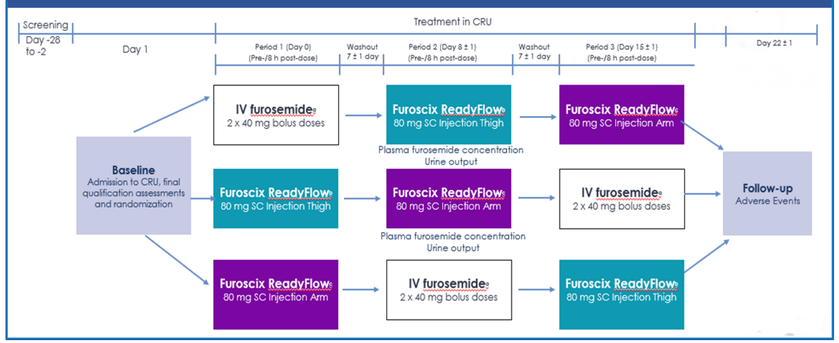
HYPOTHESIS

FUR SC administered in the thigh or upper arm has similar bioavailability to IV furosemide with similar PK and PD. Primary objective of study was to assess bioavailability of FUR SC in the thigh or upper arm vs. IV furosemide. Secondary objectives were to characterize pharmacokinetics (PK), pharmacodynamics (PD), and safety.

METHODS

- Open-label, single-center, single dose, randomized, three-way crossover study.
- Plasma concentrations, urine output (UO), and urinary sodium (Na) excretion were collected for 8 h post dose.
- Relative BA was assessed using geometric mean ratios for AUC_{last} and AUC_{inf} with BE defined if 90% CIs were within 80-125%. Safety was assessed through Day 7 ± 1 after the final treatment sequence.

Figure 1. Study Design



[a] Treatment A: IV furosemide administered as two, 40 mg doses (over 2 minutes) 2 hours apart (80 mg total dose)
[b] Treatment B: Furoscix ReadyFlow 80 mg SC administered into the Thigh via an autoinjector
[c] Treatment C: Furoscix ReadyFlow 80 mg SC administered into the upper Arm via an autoinjector

RESULTS

- 19 participants completed the study; 17 were evaluable for PK and PD analysis.
- FUR SC achieved BE relative to FUR IV at both sites, with mean (90% CI) relative BA of 91.3% (90% CI: 86.3-96.6) (thigh) and 92.7% (90% CI:88.3-97.2) (upper arm).
- Mean UO and urinary Na excretion from 0-8 h were similar across arms.
- Cumulative UO and Na increased rapidly over 3 h, then plateaued by ~6 h.
- Four adverse events (AEs) occurred: 3 after FUR IV (dizziness ×2, muscle spasm) and 1 after FUR SC upper arm (syncope, unrelated).
- All AEs were mild and resolved without intervention.

Table 1. Summary of Pharmacokinetic Parameters

	SC Furoscix ReadyFlow Thigh (n=17)	SC Furoscix ReadyFlow Arm (n=17)	IV furosemide (n=17)
C_{max} (ng/mL)	3980 ± 761	4159 ± 1227	9151 ± 2428
AUC_{last} (hr*ng/mL)	10639 ± 3280	10754 ± 3325	11933 ± 4327
AUC_{inf} (hr*ng/mL)	11101 ± 3645	11267 ± 3752	12233 ± 4685
$T_{1/2}$ (hr) [median] (min, max)	1.71 ± 0.27	1.75 ± 0.36	1.42 ± 0.22
CL/F* (L/hr)	7.84 ± 2.3	7.71 ± 2.18	7.19 ± 2.01
V_d (L)	NA	NA	14.3 ± 3.22

Values are reported in mean (SD). *CL/F is shown for furosemide 80 mg/mL SC injection. CL is shown for furosemide 80 mg IV.

Figure 3. Hourly Urine Output and Sodium Excretion

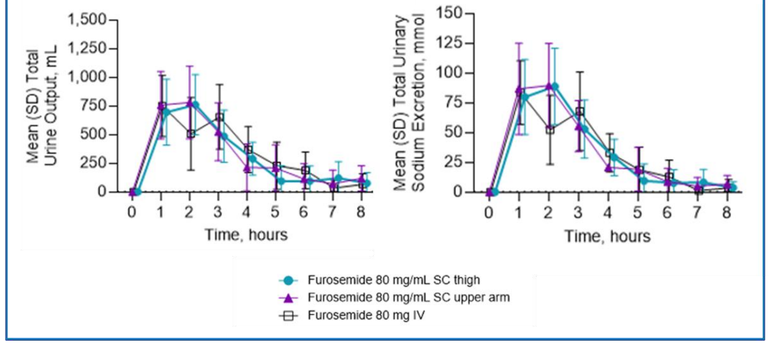


Figure 2. Primary Pharmacokinetic Endpoints

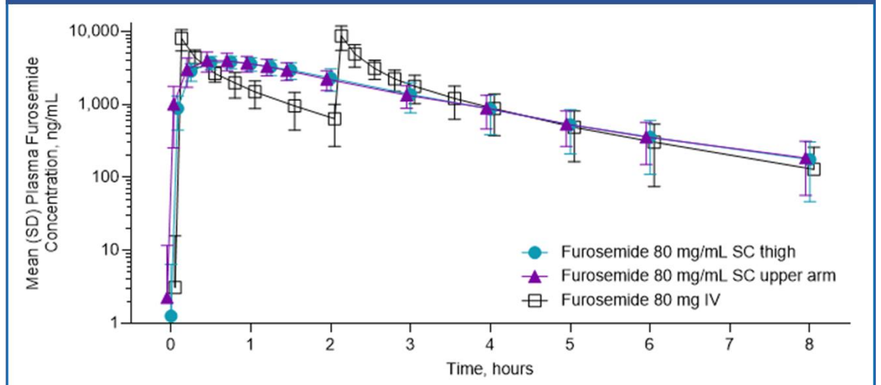
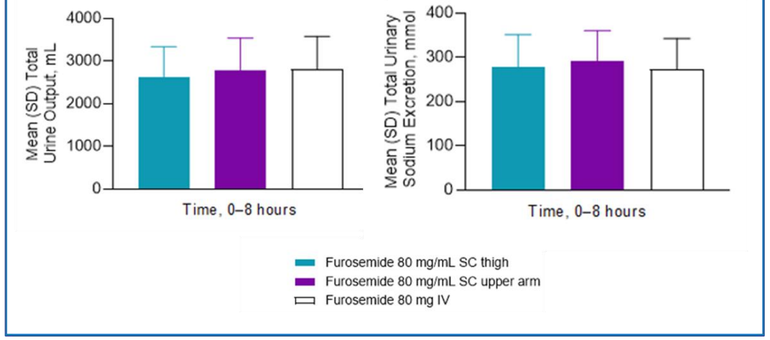


Figure 4. Cumulative Urine Output and Sodium Excretion



CONCLUSIONS

- FUR SC administered to the thigh or upper arm met the pre-determined BE criteria for AUC compared to FUR IV at both injection sites, with similar diuresis and natriuresis
- FUR SC at either site was safe and well tolerated, supporting a site-independent SC alternative to IV delivery for volume overload management.

ACKNOWLEDGEMENTS Katie Luepke, PharmD, BCPS and Sharyse Watanabe, PharmD provided medical writing support

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AUC_{inf}, area under the plasma concentration versus time curve from time zero extrapolated to infinity; AUC_{last}, area under the plasma concentration versus time curve from time zero to the time of the last measurable concentration; CL/F, apparent systemic clearance for Furoscix ReadyFlow; C_{max}, maximum observed plasma concentration; CRU, clinical research unit; F, absolute bioavailability; h, hour; IV, intravenous; SC, subcutaneous; SD, standard deviation; $t_{1/2}$, terminal-phase half-life; V_d, systemic volume of distribution