



Pharmacodynamics (PD) of a Subcutaneous (SC) Injection of a Novel-Formulation of Furosemide (FUR)

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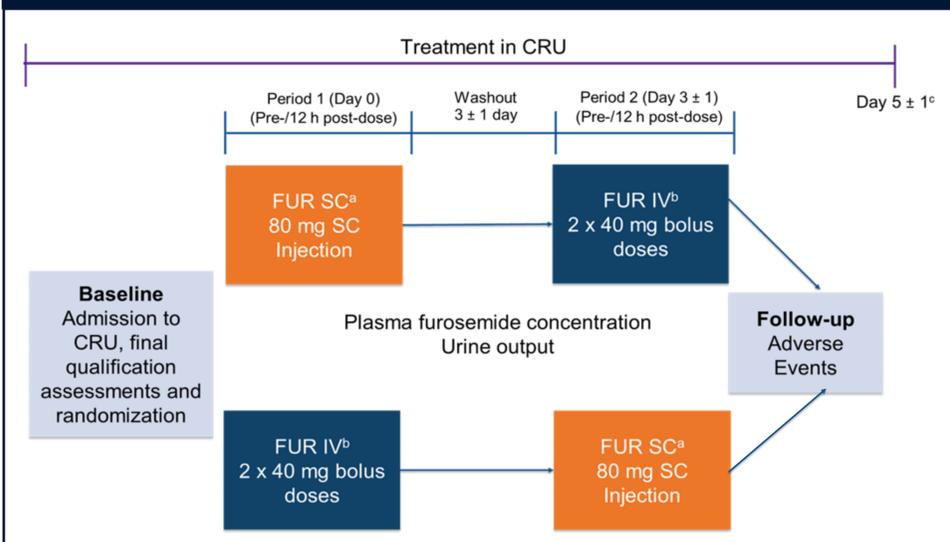
INTRODUCTION AND OBJECTIVES

- Furoscix 80 mg/10 mL is a buffered formulation of FUR that is self-administered SC via an On-body Infusor over 5 hrs.
- SCP-111 (FUR SC) is a novel-formulation of FUR 80 mg/mL currently in development that is administered as an SC injection.
- FUR SC demonstrated 107.3% relative bioavailability to furosemide IV; [90% CI 103.9, 110.8] with similar urine output (UO) and Na excretion at 6, 8 and 12 hours¹.
- The purpose of this analysis was to explore pharmacokinetics (PK) and PD of FUR SC, notably hourly UO and Na excretion, and the relationship between furosemide plasma concentration and effect.

METHODS

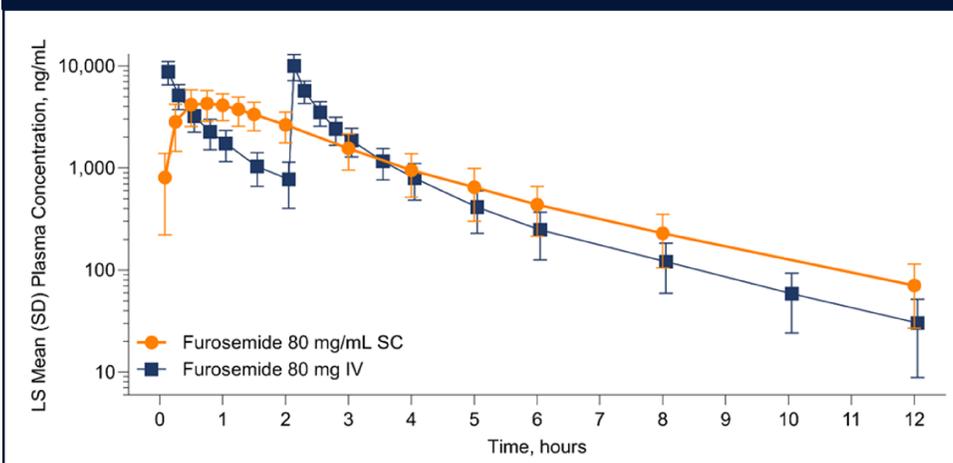
- Post-hoc analysis of open-label, single center, single dose, randomized two-way (two period) crossover study in healthy participants (Figure 1).
- Blood was collected pre-dose and for 12 hours post-dose to determine FUR plasma concentrations.
- Urine was collected for 12 hours post-dose to determine urine output (UO) and urinary Na excretion.
- Mean hourly UO and Na excretion from FUR SC and FUR IV were plotted against time (hours) across the 12-hour study period.
- Mean hourly UO and Na excretion were subsequently plotted against FUR concentrations from SC and IV, and best-fit curves were generated to determine respective UO and Na excretion thresholds.

Figure 1. Study Methodology



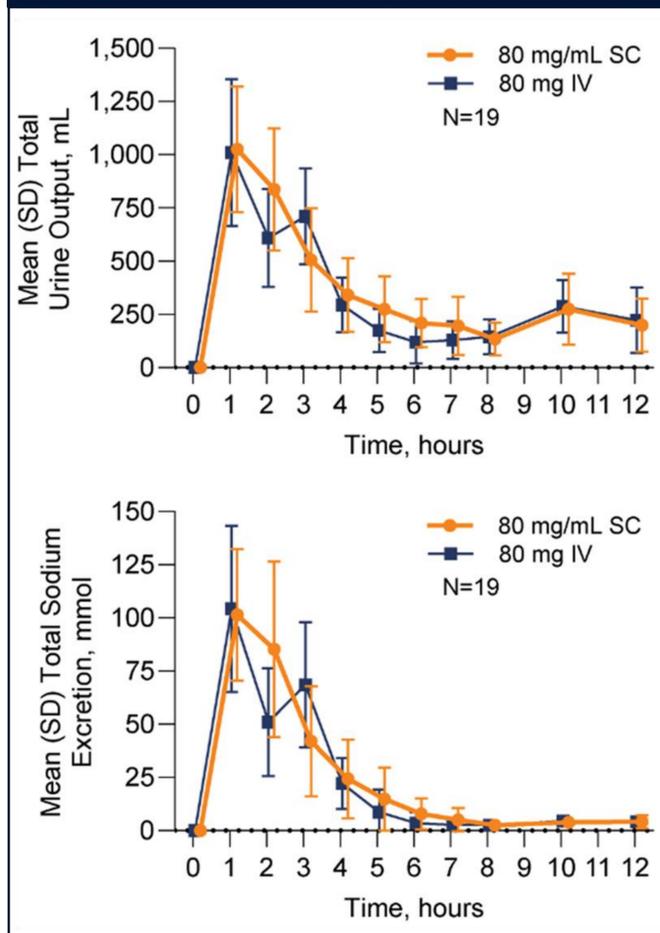
^a SCP-111 80 mg SC administered via an autoinjector; ^b Furosemide IV administered as two, 40 mg doses (over 2 minutes) 2 hours apart (80 mg total dose); ^c Follow-up visit should occur 24-48 hours after discharge from CRU for Crossover Period 2; CRU=clinical research unit.

Figure 2. Least-Squares Mean Plasma Furosemide-Concentration-Versus Time Curve



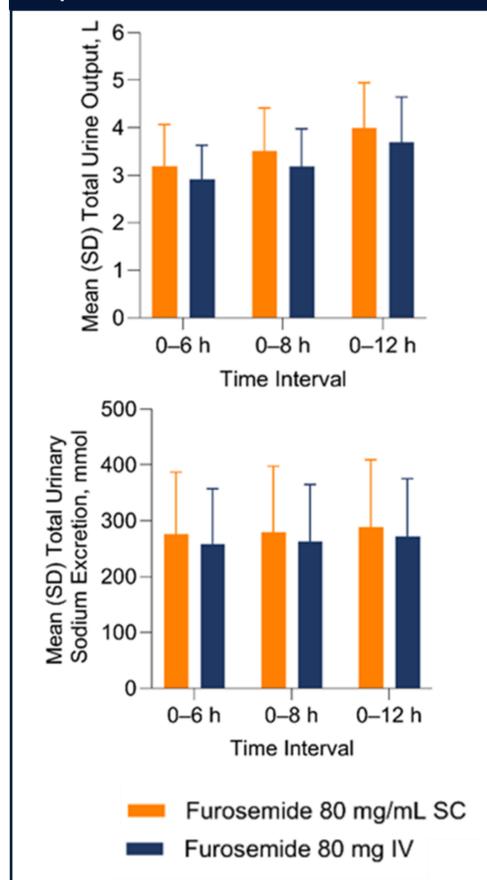
IV, intravenous; LS, least squares; SC, subcutaneous; SD, standard deviation.

Figure 3. Hourly Mean (SD) Urine Output and Sodium Excretion



IV, intravenous; SC, subcutaneous; SD, standard deviation.

Figure 4. Mean (SD) Post-Dose Total Urine Output and Sodium Excretion

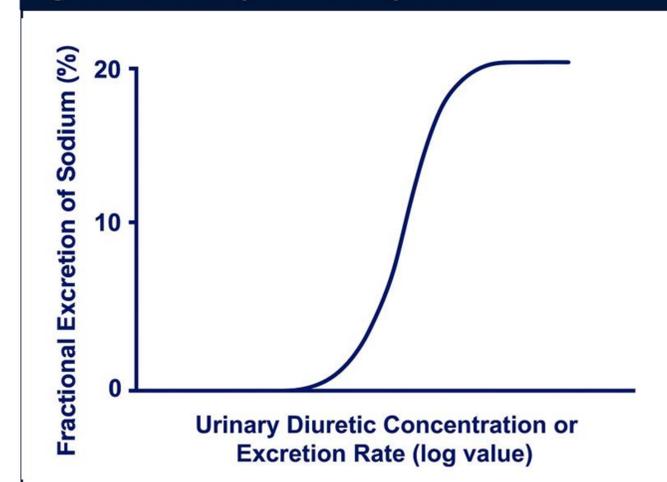


IV, intravenous; SC, subcutaneous; SD, standard deviation.

RESULTS

- 21 subjects were randomized and 19 had sufficient sample estimation of PK and PD parameters.
- 71.4% female; BMI, 27.4 (19.3, 51.4) kg/m²; eGFR, 79 (56, 138) mL/min/1.73 m²
- Figure 2 illustrates the concentration vs. time curve for both FUR SC and FUR IV.
- Mean (SD) UO and Na excretion peaked at 1 hour for both FUR SC [1026.1 (295.5) mL and 101.4 (30.8) mmol] and FUR IV [1011.6 (346.1) mL and 104.3 (39.0) mmol] and was consistent between routes over the 12-hour duration (Figure 3).
- There was no statistically significant difference between furosemide 80 mg/mL SC injection and furosemide 80 mg IV in diuresis or natriuresis at 0-6 hours, 0-8 hours, or 0-12 hours (Figure 4).
- A sigmoidal concentration-response curve was observed for both mean hourly UO and Na excretion, which is consistent with the established general pharmacology of loop diuretics (Figure 5).

Figure 5. Pharmacodynamics of Loop Diuretics



Adapted from: Brater DC. NEJM 1998;339(6):387-95.

SUMMARY AND CONCLUSIONS

- FUR SC demonstrated similar hourly and cumulative diuresis and natriuresis over the 12-hour period compared to FUR IV.
- Plasma furosemide concentrations from both SC and IV administration correlated with UO and Na excretion, which is consistent to that reported in the literature.
- Furosemide 80 mg/mL administered as a SC injection is a potential alternative to IV administration, with similar PK and PD.