EFFECT OF SUBCUTANEOUS FUROSEMIDE (FUROSCIX® **(furosemide) 80 mg/10mL for subcutaneous administration**) ON NATRIURETIC PEPTIDES, QUALITY OF LIFE AND PATIENT/CAREGIVER SATISFACTION IN HEART FAILURE PATIENTS: SECONDARY OUTCOMES OF THE FREEDOM-HF TRIAL

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Cycle of Decompensation and Hospitalization is the Primary Burden for Patients Suffering from HF

Stable patient treated with oral diuretic

- Fluid retention (Congestion) – hallmark of HF
- Decompensation leads to ↓ oral bioavailability diuretics
- Worsening symptoms is the most common reason patients contact their provider

Hospitalized patient treated with IV diuretic

- 59% of hospital admission directly attributed to volume overload[1]
- Up to 50% of HF hospital admissions may be avoidable[2]
- 30 – 50% patients discharged still congested[3-5]
- 25-30% of patients readmitted to the hospital after discharge within 30 days[6,7]

1. Bennett S, et al. American Journal of Crit Care. 1998;7(3):168-174. 2. Collins et al. J Am Coll Cardiol. 2013 January 15; 61(2): 121-126. 3. Neuenschwander JF, et al. Crit Care Clin. 2007;23(4):737-58. 4. Costanzo MR, et al. Am Heart J. 2007;154(2):267-77. 5.Fonarow GC, et al. JAMA. 2005;293(5):572-80 6. Kilgore M et al. *Risk Manag Healthc Policy*. 2017;10:63..7. . Fitch K, et al (2017) The cost burden of worsening heart failure in the Medicare fee for service population: an actuarial analysis [white paper]

FUROSCIX® Delivery System Incorporates an On-Body Infusor

Incorporates West Pharmaceutical Services, Inc.'s SmartDose® Gen II 10ml platform technology

Technology is FDA and EMA approved as part of a combination product

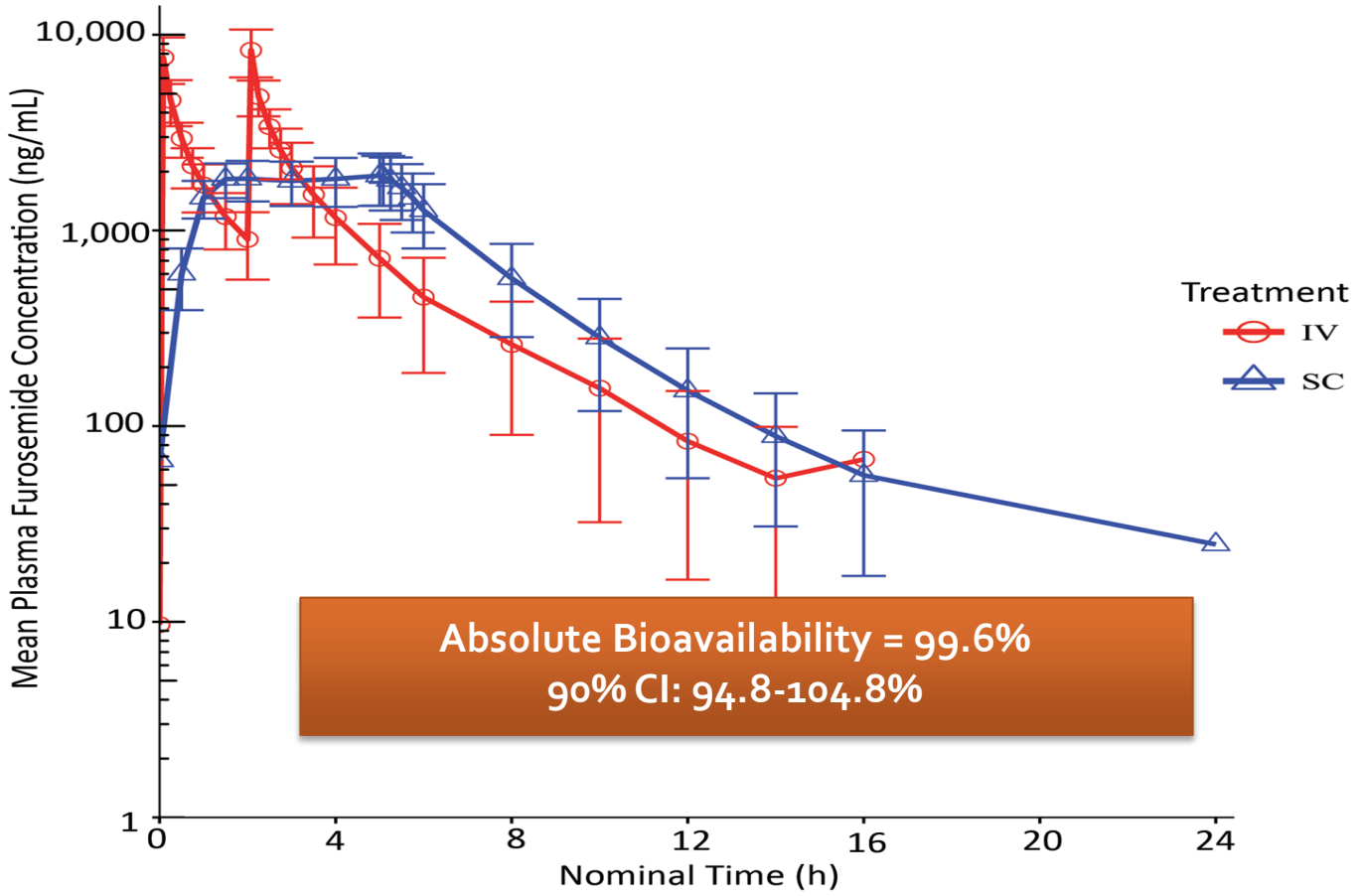
- Pre-filled Crystal Zenith® disposable cartridge
- Delivers fixed 80mg sc dose through pre-programmed, biphasic profile (30mg first hour + 12.5mg/hour for next 4 hours)
- Visual, tactile, and audible feedback
- Electromechanical drive
- Patient-centric design
- Wireless connectivity capability

For Illustrative Purposes Only

Pivotal PK / PD Study:
IV vs SC Furosemide Concentration-Time Profile

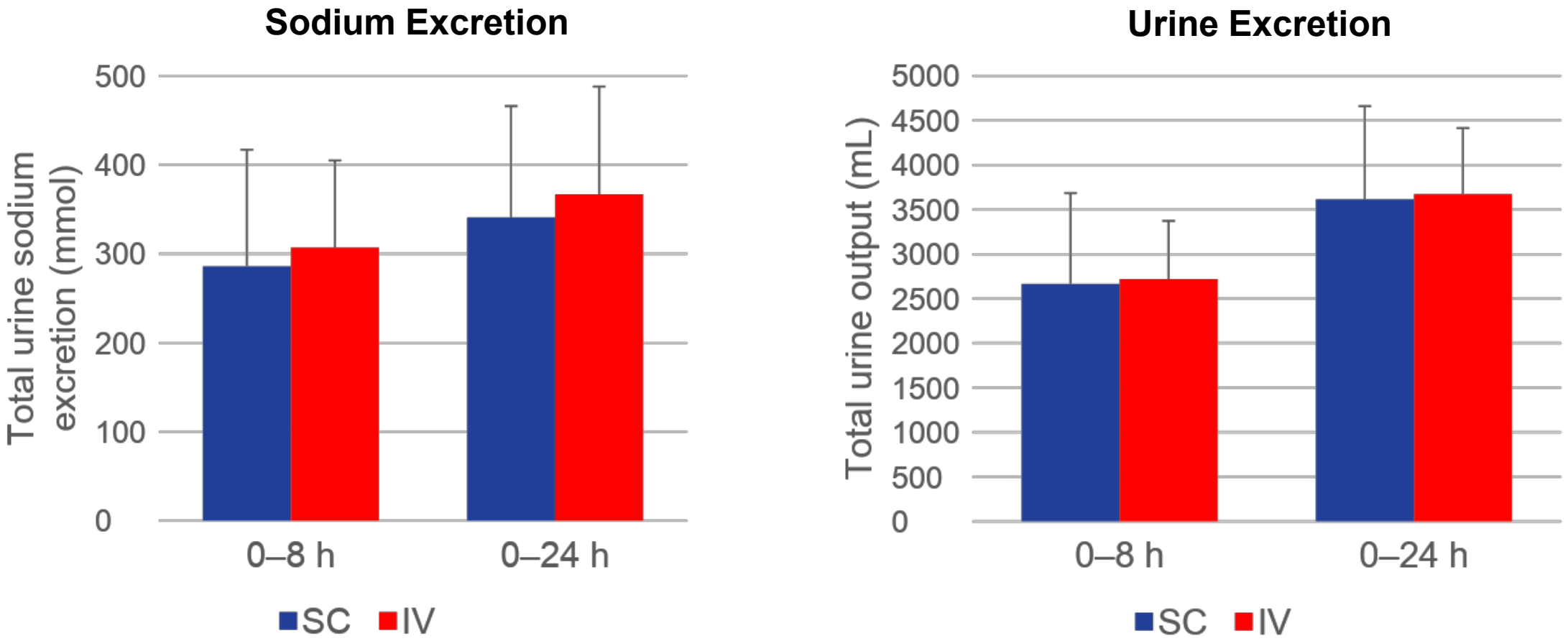
	SC Administration (n = 15)[a]	IV Administration (n = 15)[a]
C_{max}, ng/mL Mean ± SD	2040 ± 449	8580 ± 2540
t_{max}, h Median (min–max)	4.00 (1.00–5.08)	2.08 (0.08–2.08)
AUC_{last}, h*ng/mL Mean (SD)	13000 ± 4000	13000 ± 4050
AUC_{∞}, h*ng/mL Mean (SD)	13100 ± 4010	13200 ± 4170

[a] One subject was excluded from analysis due to high pre-dose concentration of furosemide.



Sica DA, et al. JACC: Basic to Translational Science. 2018.

Pivotal PK / PD Study:
Pharmacodynamics



CI, confidence interval; h, hour; IV, intravenous; SC, subcutaneous; SD, standard deviation.

Sica DA, et al. JACC: Basic to Translational Science. 2018.

FREEDOM-HF

Study Overview

GOAL: To evaluate the economic impact and safety of initial hospital avoidance in heart failure patients presenting to the emergency department with worsening congestion who are treated with FUROSCIX outside the hospital

Objectives

- Compare differences in healthcare resource utilization and costs for patients treated with FUROSCIX outside the hospital with patients receiving IV furosemide inside the hospital
- Evaluate the safety of FUROSCIX administered outside the hospital
- Describe the quality of life and patient satisfaction for patients who receive FUROSCIX outside the hospital

Study Design

- Open-label, prospective, case-control study
- Patients discharged from the emergency department (ED) and received FUROSCIX at home
- Cost differences derived and calculated from IBM MarketScan Commercial Claims and Medicare Supplemental Database (2018-2019) and matched (1:1 to 4:1) to FUROSCIX group
  - Subjects admitted to the hospital for ≤ 72 hours
  - Comorbidities consistent with inclusion/exclusion criteria
  - Matched to 7 variables associated with HF hospitalizations

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FREEDOM-HF:
Key Entry Criteria

- Age 18-80 years w/ NYHA Class II-III HF presenting to the ED for worsening HF
- On background oral diuretic therapy (40-160mg furosemide equivalents daily)
- Signs of extracellular volume expansion defined as one or more of the following
  - JVD, pitting edema, abdominal distension, pulmonary congestion on chest x-ray, rales
- After initial ED evaluation and treatment, all of the following
  - Oxygen saturation ≥ 90% on exertion, Respiratory Rate < 24 breaths per minute, Resting Heart Rate < 100 beats per minute, Systolic Blood Pressure > 100 mmHg
- Creatinine clearance > 30 mL/min and no evidence of acute renal failure as determined by investigator
- Adequate environment for at home administration of parenteral diuretics

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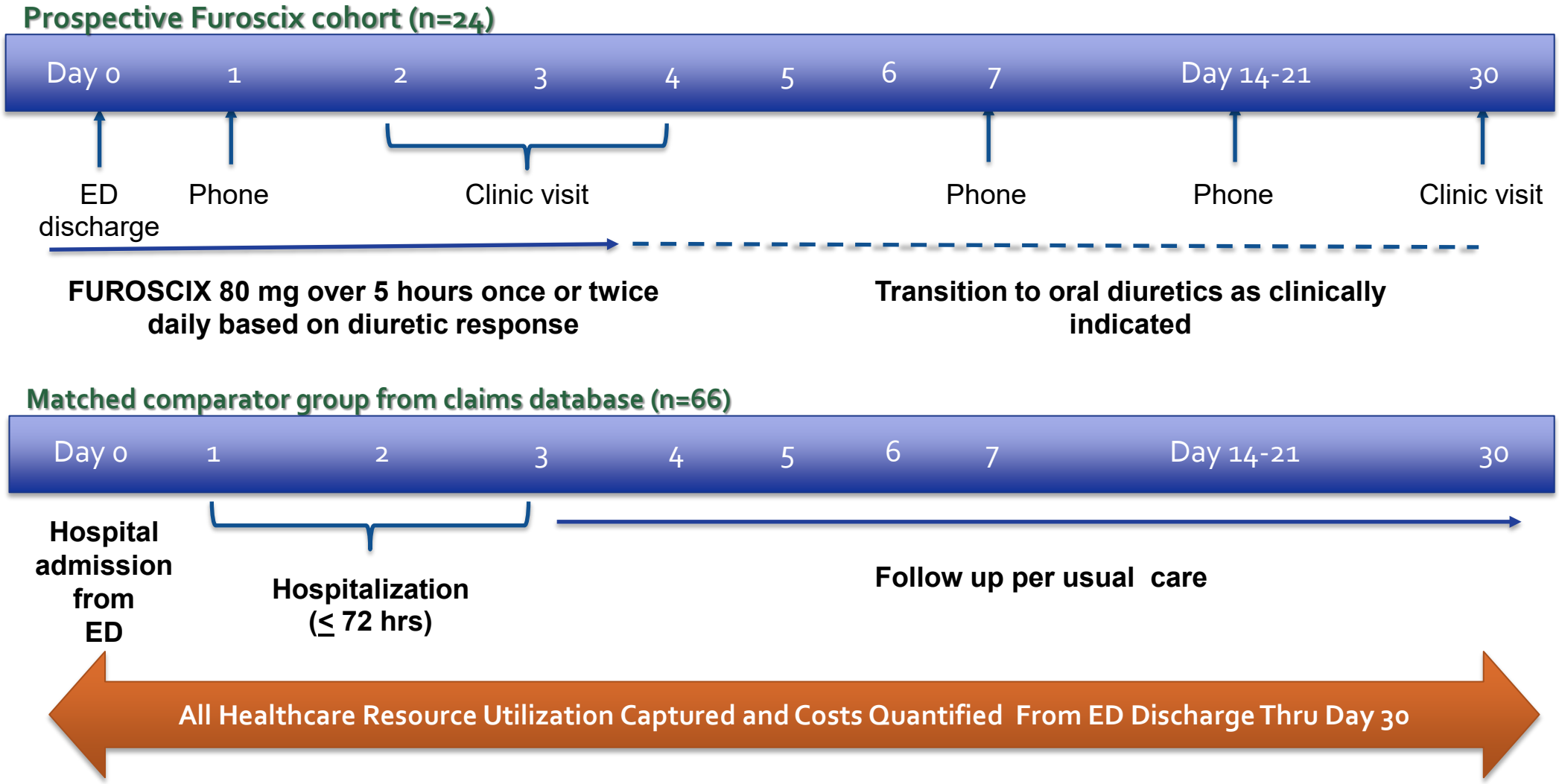
FREEDOM-HF
Study Design



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FREEDOM-HF
Matching Demographics and Baseline Characteristics

Characteristic	Overall (N=90)	Furoscix (n=24)	Comparator (n=66)	p-value
Age (mean (SD)	57.1 (8.32)	56.3 (12.29)	58.0 (6.39)	0.508
Sex (M/F), n (%)*	57 (62.5%)/33 (37.5%)	15 (62.5%)/9 (37.5%)	42 (62.5)/24 (37.5)	>0.9999
Ejection Fraction (n (%))*				>0.9999
Systolic (HFrEF)	39 (45.8%)	11 (45.8%)	28 (45.8%)	
Diastolic (HFpEF)	39 (41.7%)	10 (41.7%)	29 (41.7%)	
Combined HFrEF & HFpEF	12 (12.5%)	3 (12.5%)	9 (12.5%)	
History of Chronic Kidney Disease (n (%))*				>0.9999
No history	62 (70.8%)	17 (70.8%)	45 (70.8%)	
Stage 2 CKD	5 (4.2%)	1 (4.2%)	4 (4.2%)	
Stage 3 CKD	23 (25%)	6 (25%)	17 (25%)	
HF hospitalizations 6 months prior to baseline (n (%))*				0.4284
None	47 (41.7%)	9 (37.5%)	38 (45.8%)	
≥ 1	43 (58.3%)	15(62.5%)	28 (54.2%)	
Chronic Obstructive Pulmonary Disease (COPD) (n (%))*	33 (30.6%)	6 (25%)	27 (36.1%)	0.2575
Diabetes (n (%))*	62 (58.2%)	12 (50%)	50 (66.3%)	0.1192

* Weighted mean, SD and % are based on count of comparator patients within each Furoscix match set (i.e. 1/k, where k=1, 2, 3 or 4). Weighting does not apply to Furoscix patients.

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Furoscix Baseline Patient Characteristics and HF Medications

Variable	Furoscix (n=24)
Age, mean (SD)	56 (12)
Males, n (%) [a]	15 (63)
BMI, kg/m². mean (SD) (n=23)	44 (14)
Weight, kg, mean (SD)	131 (40)
Serum creatinine, mg/dL, mean (SD)	1.35 (0.4)
eGFR (MDRD), mean (SD)	61 (24)
BNP (pg/mL), mean (SD) (n=12)	785 (1130)
NT-proBNP, mean (SD) (n=11)	823 (1044)
Heart failure	
Systolic HF	11 (46)
Diastolic HF	10 (42)
Combined	3 (13)
History of chronic kidney disease (CKD)	
No history of CKD, n (%)	17 (71)
CKD Stage 2	1 (4)
CKD Stage 3	6 (25)
≥ 1 HF Hospitalization within 6 months	15 (63)

Variable	Furoscix (n=24)
Diabetes, n (%)	12 (50)
COPD, n (%)	6 (25)
Prior MI, n (%)	2 (8)
Hypertension, n (%)	22 (92)
Hyperlipidemia, n (%)	15 (63)
Arrythmia, n (%)	12 (50)
Valvular disease, n (%)	7 (29)
Unstable angina, n (%)	6 (25)
Daily furosemide equivalents (mg), mean (SD) (n=23)*	139 (98)
Furosemide, n (%)	12 (50)
Bumetanide, n (%)	4 (17)
Torsemide, n (%)	7 (29)
None, n (%) *	1 (4)
Metolazone, n (%)	5 (21)
Beta blockers, n (%)	15 (63)
ARNI/ACEi/ARB, n (%)	11 (46)
Nitrate, n (%)	4 (17)
Aldosterone antagonist, n (%)	10 (42)
Hydralazine, n (%)	6 (25)

FREEDOM-HF
Primary Outcome: Healthcare Costs

Outcome	Furoscix[b] (n=24)	Comparator (n=66)	Difference (95% CI)	P-value[a]
HF-related health care costs, mean (SD)	$2920.30 (7073.20)	$19,915.60 (10,666.60)	-$16,995.30 (-22,187.90, -11,802.70)	<0.0001
HF-related health care costs, median (Q1, Q3)	$1,374.90 (1374.90, 1555.00)	$15,182.00 (12,658.10, 17,691.70)	-$13,807.10 (-16,846.50, -13,476.30	<0.0001
Overall health care costs, mean (SD)	$7512.30 (11,905.50)	$35,352.80 (31,662.00)	-$27,840.50 (-41,581.10, -14,100.00)	<0.0001
Overall health care costs, median (Q1, Q3)	$1735.20 (1555.00, 7196.90)	$17,691.70 (15,209.60, 21,071.20)	-$15,956.60 (-16,729.10, -12,908.10)	<0.0001

Abbreviations: Heart Failure (HF); Standard Deviation (SD) [a] P-value was obtained from the t-test statistic. [b] Costs in Furoscix arm does not include a cost for Furoscix

All 24 patients in the Furoscix group avoided the initial HF hospitalization

30 Day HF hospitalization: 1/24 (4.2%) Furoscix group vs. 7 (10.6%) Comparator group

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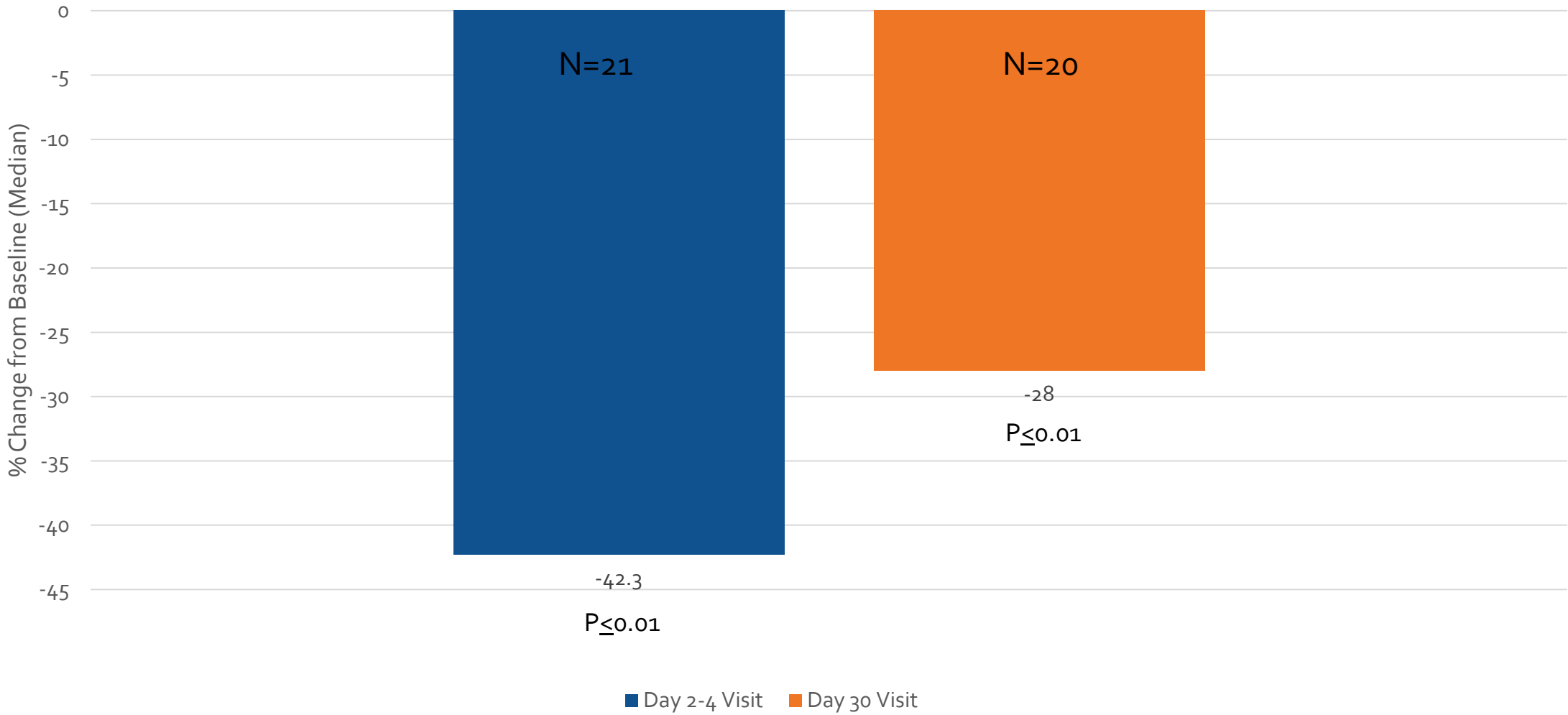
FREEDOM-HF

Secondary Outcome: Median Percent Change in BNP or NT-proBNP from Baseline



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FREEDOM-HF
Secondary Outcome: Health-related Quality of Life (KCCQ-12)

Score	Furoscix (n=24)			
	Baseline	Day 30 visit	**Difference (95% CI)**	**p-value**
Summary Score, mean (SD)	**29.9 (22.8)**	**42.8 (28.4)**	**12.8 (0.4, 25.3)**	0.0443
Physical Limitation Score, mean (SD)	37.1 (30.1)	43.7 (32.0)	6.5 (-10.4, 23.4)	0.4328
Symptom Frequency Score, mean(SD)	**33.1 (28.6)**	**50.5 (32.3)**	**17.4 (6.1, 28.8)**	0.0041
Quality of Life Score, mean (SD)	27.1 (28.0)	35.9 (29.8)	8.9 (-4.2, 21.9)	0.1743
Social Limitation Score, mean (SD)	29.0 (26.1)	40.9 (31.3)	11.9 (-2.5, 26.4)	0.1006

Scores are scaled 0-100, where 0 denotes the lowest reportable health status and 100 the highest

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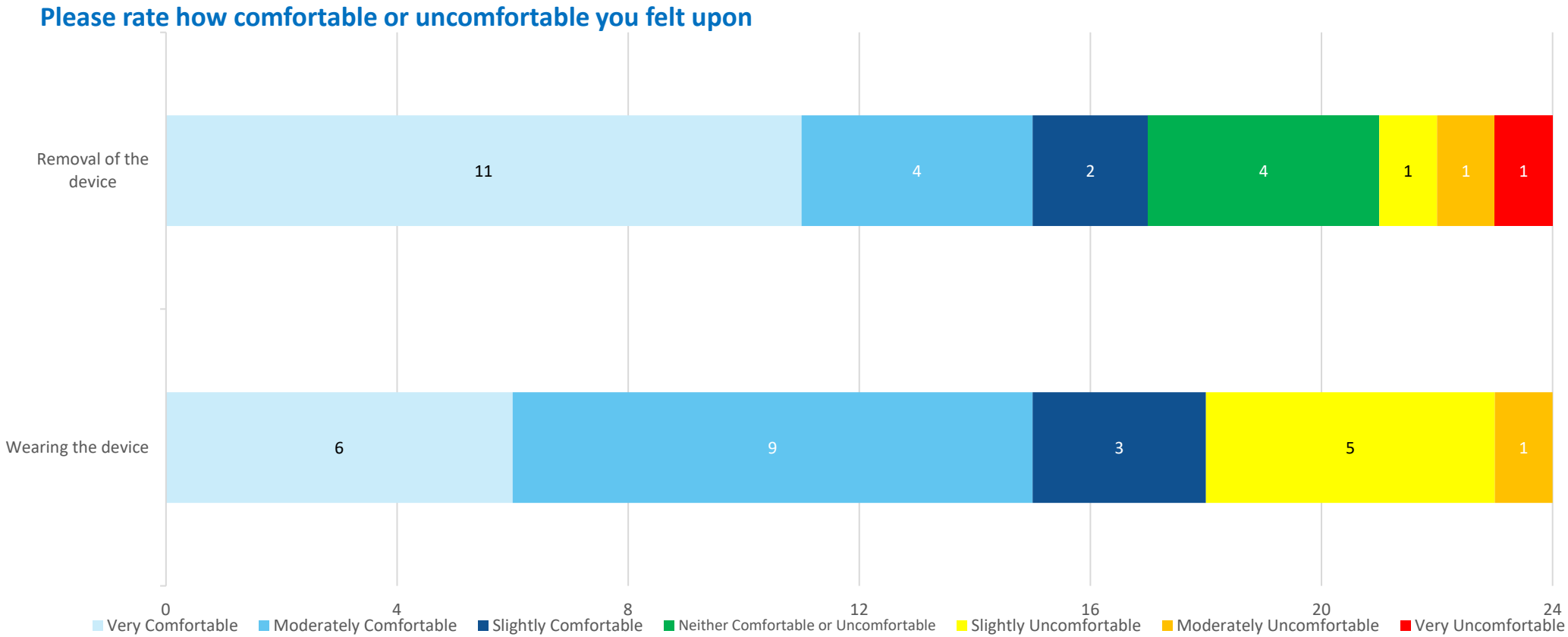
FREEDOM-HF
Comfort of Wear Questionnaire – Day 2-4

- Most (88%) of patients felt comfort or experienced no discomfort removing the device
- Most (75%) of patients felt comfortable wearing the device, with only 1 patient reporting the device as moderately uncomfortable



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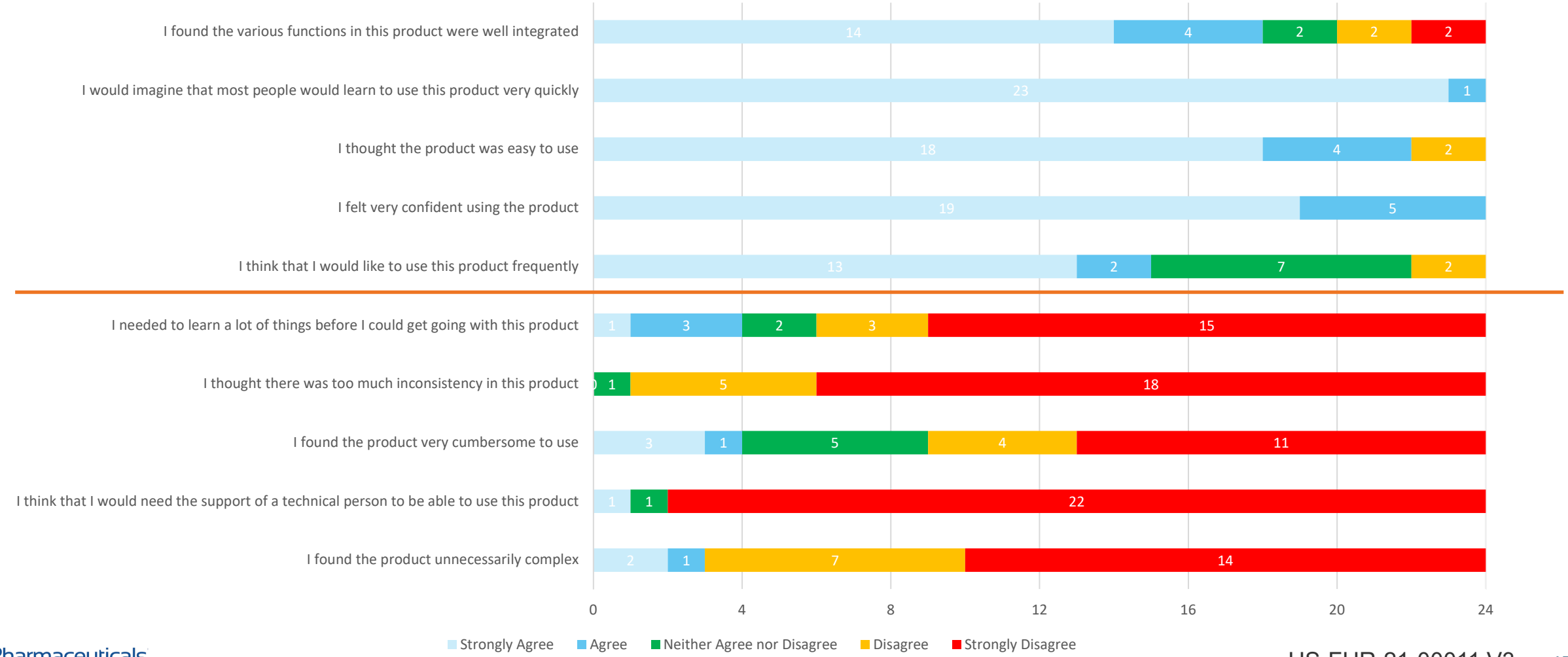
FREEDOM-HF
Subject and/or Caregiver Satisfaction

Nearly all patients were satisfied with the device and found it easy to use



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FREEDOM-HF

Safety

- Most common (>10%) adverse events (AEs) were infusion site bruising (29%), infusion site pain (29%) and dizziness (13%) – all assessed by investigator as mild in severity
- 6 subjects experienced serious adverse events (SAEs)
  - None of the SAEs were determined to be related to Furoscix
- No subjects withdrew from the study due to an AE
- No deaths

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Thank You!

References

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