

DICTATE-AHF

Efficacy and Safety of Dapagliflozin in Acute Heart Failure

NCT04298229

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On behalf of DICTATE-AHF Investigators

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Background

Two Goals for Acute Heart Failure

1) Decongestion

2) GDMT Optimization

Improve
Post-DC Outcomes

Loop + Acetazolamide			No Improvement
Loop + Thiazide			No Improvement
Loop + SGLT2i			Improved Outcomes

Background

- **Concerns of early in-hospital SGLT2 inhibitor SAFETY:**
 - Hypoglycemia
 - Ketoacidosis
 - Worsening renal function
 - Genitourinary infections
 - Questionable magnitude of diuretic and natriuretic benefit

Early addition of Dapagliflozin is a potential strategy to improve achievement of both primary AHF therapeutic goals, but efficacy and safety are unknown

DICTATE-AHF Design

- Investigator-initiated, multicenter, prospective, randomized, open-label study funded by AstraZeneca

Objective efficacy outcomes and blinded assessment of safety outcomes

- 240 Patients hospitalized with hypervolemic AHF randomized within 24 hours of presentation
 - Regardless of LVEF
 - Beginning April 2020, only patients with Type 2 diabetes mellitus were included
 - September 2021 - protocol amended to include:
 - With or without type 2 diabetes mellitus
 - $eGFR \geq 25 \text{ mL/min/1.73m}^2$

Key Inclusion Criteria

- Age of 18 years or older
- Randomized within 24 hours of presentation hypervolemic AHF:
 - ≥ 2 objective measures of hypervolemia
- Planned or current use of IV loop diuretic therapy
- $\text{eGFR} \geq 25 \text{ mL/min/1.73m}^2$

Key Exclusion Criteria

- Type 1 diabetes
- Serum glucose < 80mg/dL
- Systolic blood pressure < 90mmHg
- IV inotropic therapy
- History of diabetic ketoacidosis
- Inability to perform standing weights or measure urine output accurately

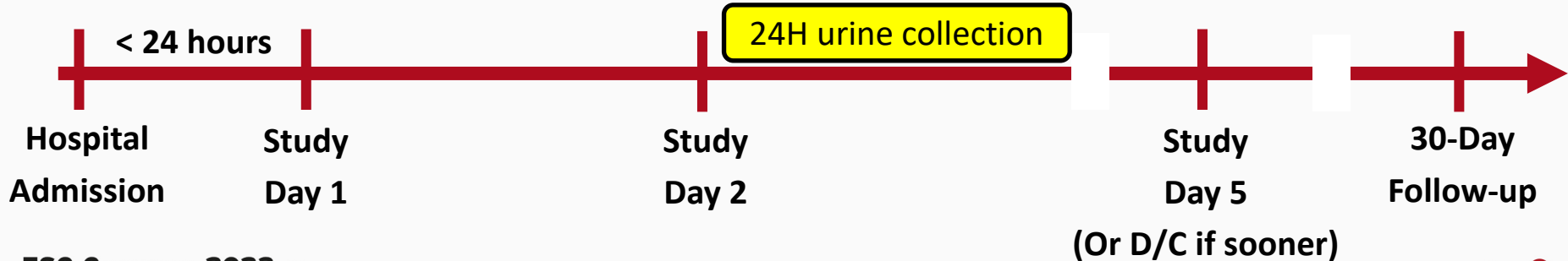
DICTATE-AHF

Dapagliflozin 10mg Daily + structured usual care
with protocolized diuretic titration (N=120)

Screening
Randomization
Baseline Assessments

IV loops titrated via protocol in both
treatment arms to Goal 3-5L UOP/day

Structured usual care with
protocolized diuretic titration (N=120)



Study Outcomes

Primary Outcome

$$\text{Diuretic Efficiency} = \frac{\text{Cumulative weight change (kg)}}{\text{Cumulative loop diuretic dose (mg)}}$$

- Calculated until Day-5 or hospital discharge if sooner
- Expressed as *kg/40mg IV Furosemide equivalents*
- Compared across treatment assignment using a proportional odds regression model adjusting for baseline weight

Study Outcomes

Secondary Outcomes adjudicated by blinded committee

- Incidence of worsening HF during hospital stay
- HF-related or diabetes-related 30-day readmissions

Safety Outcomes adjudicated by blinded committee

- Incidence of diabetic ketoacidosis
- Prolonged hospitalization for hypotension
- Prolonged hospitalization for hypoglycemia
- Change in eGFR from baseline to end-of-study

Select Exploratory Outcomes

- Measures of natriuresis and diuresis
- Hospital length of stay

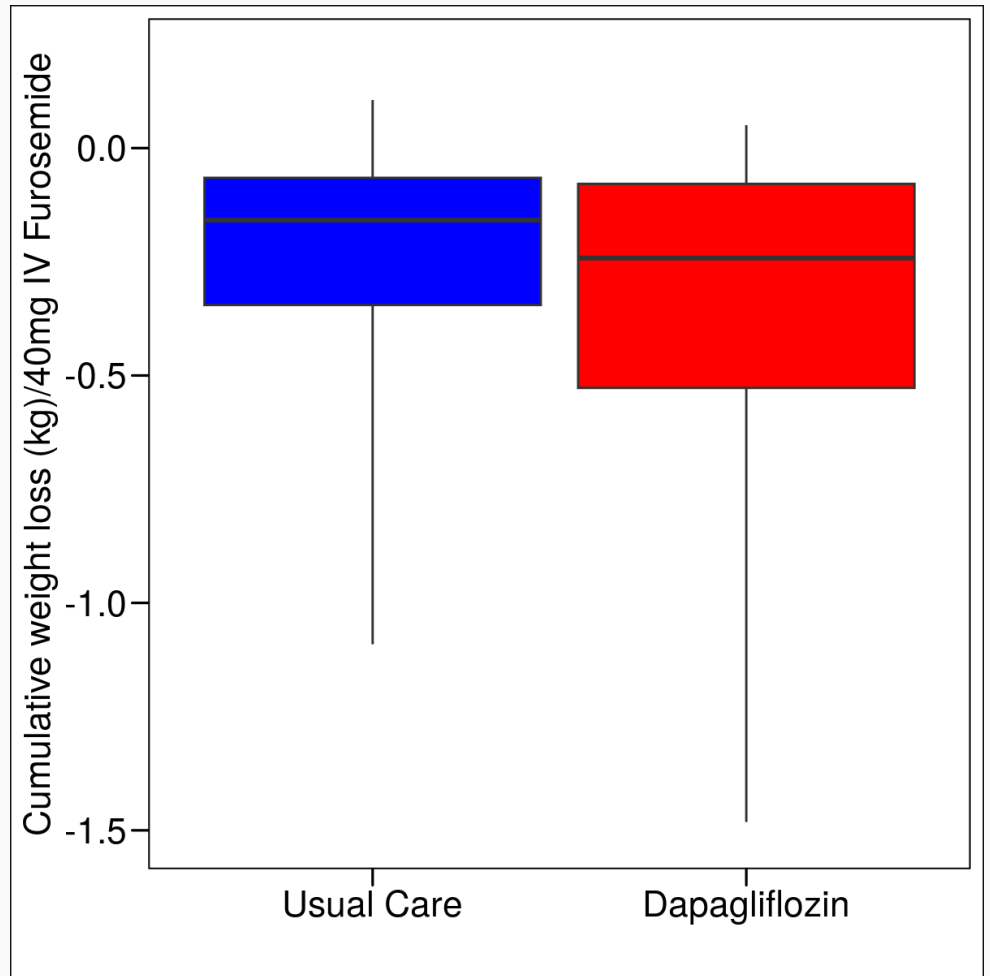
Baseline Characteristics

Characteristic	Total Population (N=238)	Usual Care (N=119)	Dapagliflozin (N=119)
Age (yrs)	65 (56 – 73)	64 (55 – 74)	65 (56 – 73)
Male Sex	61%	56%	66%
White Race	68%	71%	66%
T2DM	71%	71%	71%
LVEF ≤ 40%	52%	55%	48%
SBP (mmHg)	121 (110 – 136)	120 (110 – 136)	121 (112 – 136)
eGFR (mL/min/1.73m ²)	53 (42 – 70)	54 (40 – 71)	51 (43 – 68)
IV furosemide dose prior to randomization (mg)	80 (40 – 140)	80 (80 – 120)	80 (40 - 160)

Primary Outcome

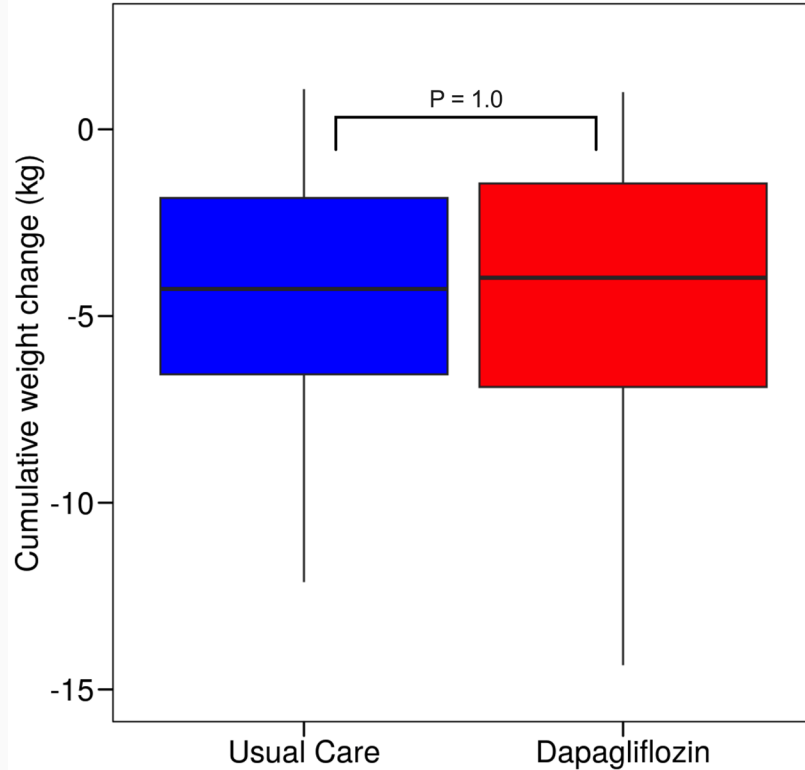
**Adjusted Odds Ratio 0.65
(95% CI 0.41 – 1.01); P=0.06**

**Unadjusted Odds Ratio 0.64
(95% CI 0.41 – 1.00)**

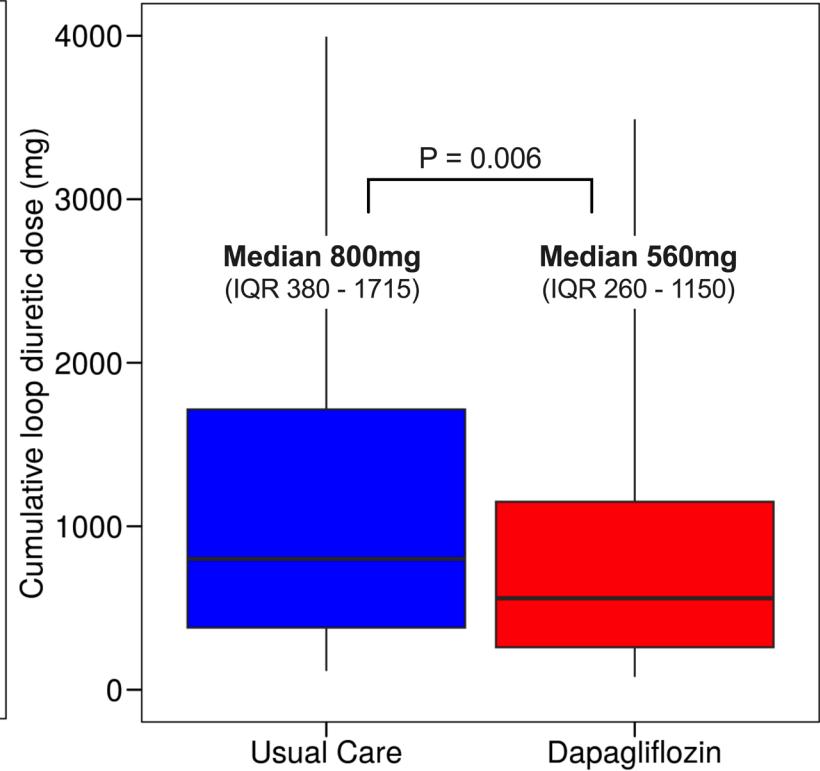


Primary Outcome Components

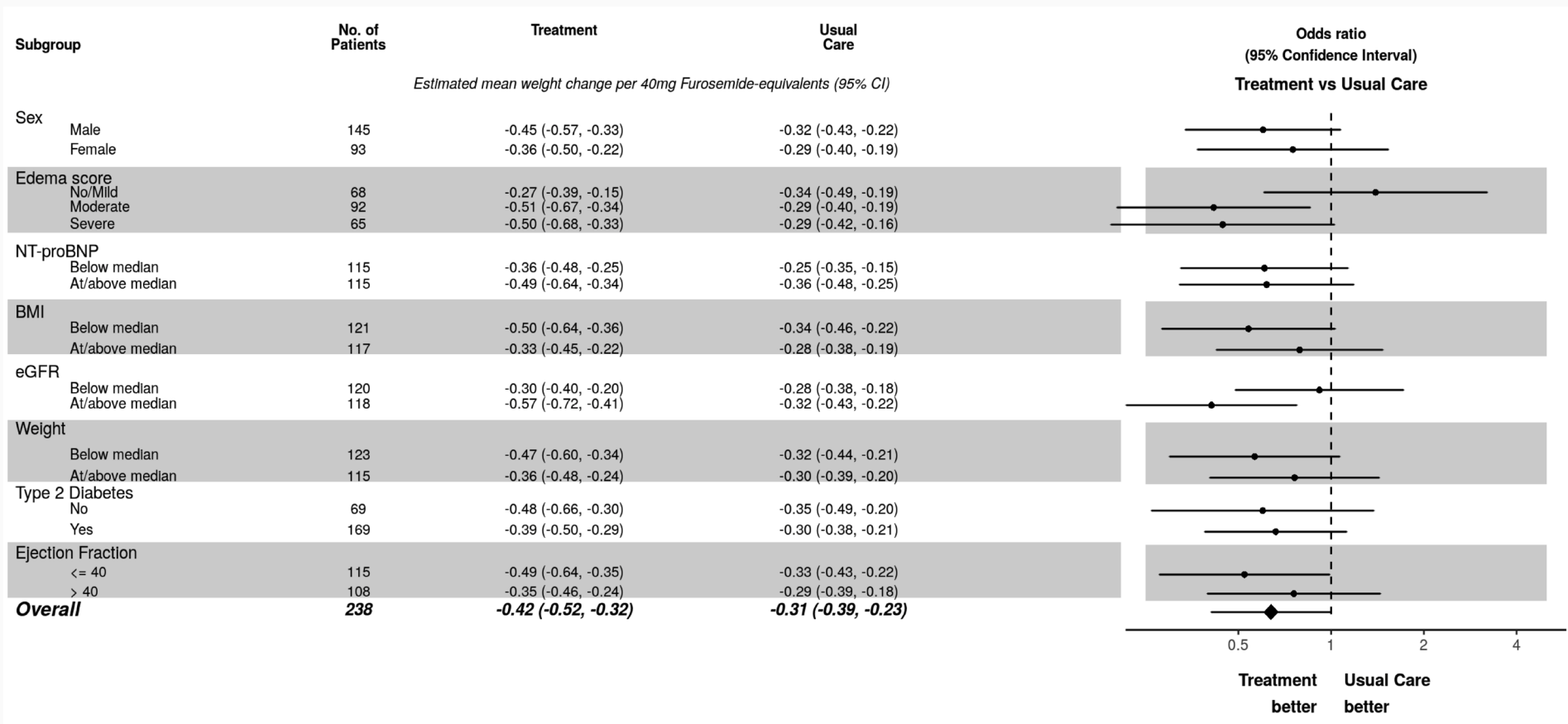
Cumulative Weight Change



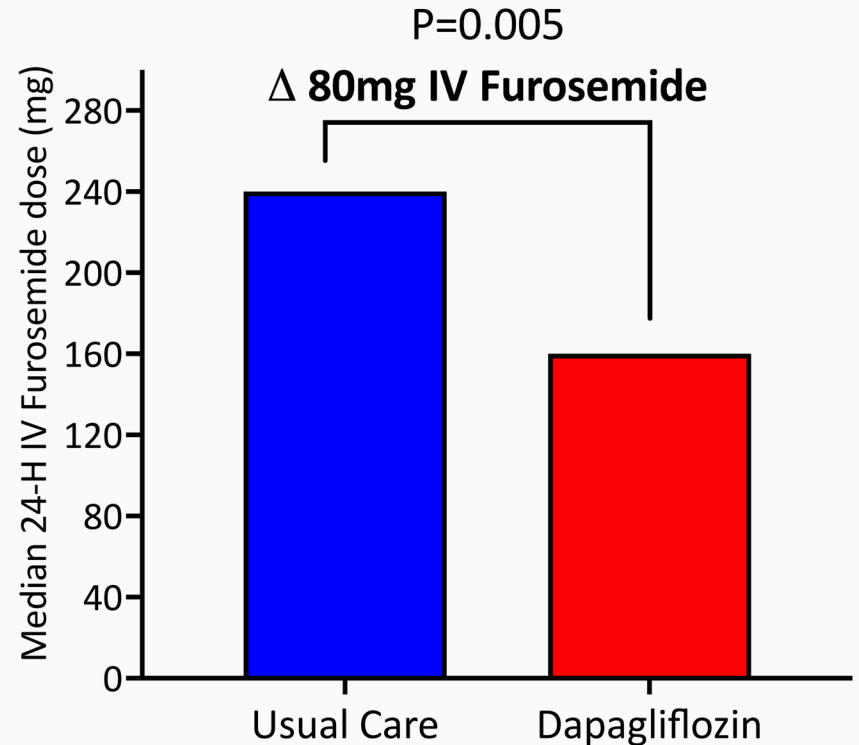
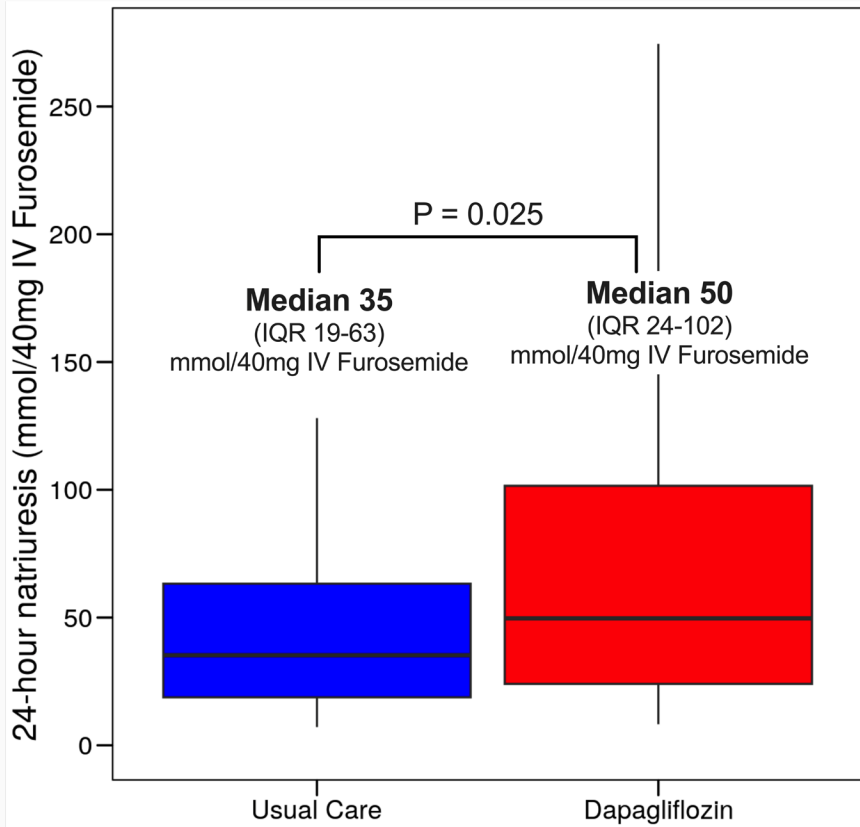
Cumulative Loop Diuretic Dose



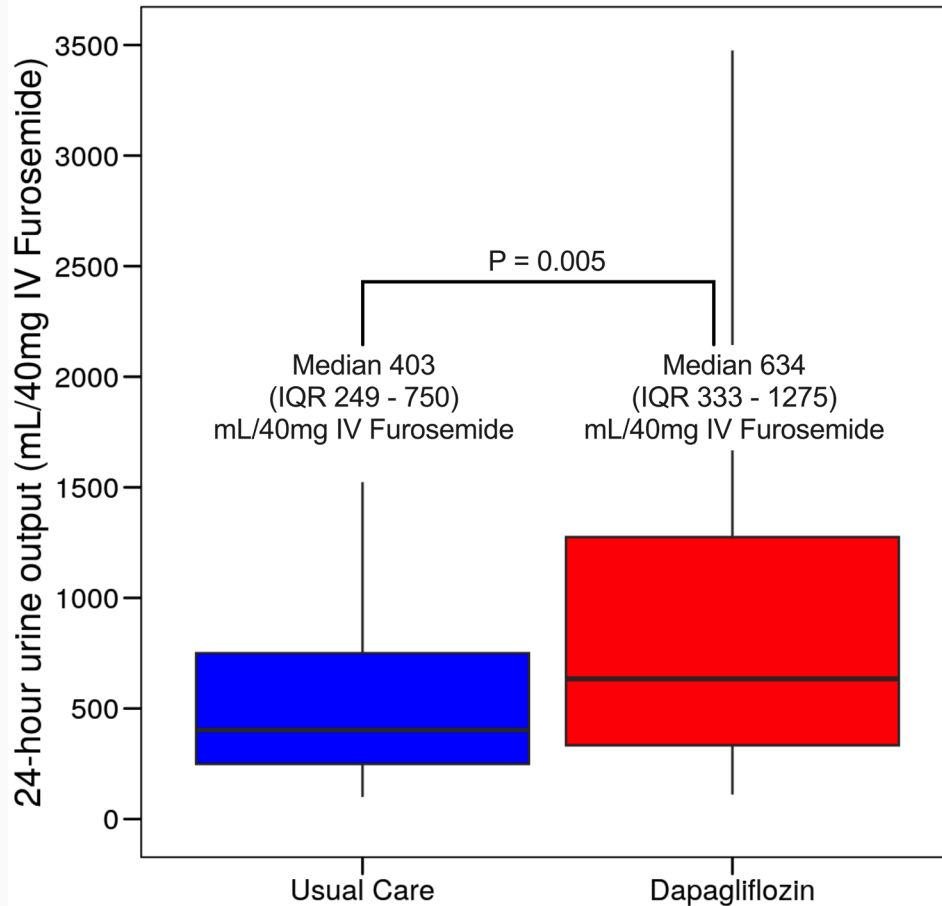
Heterogeneity of Treatment Effect



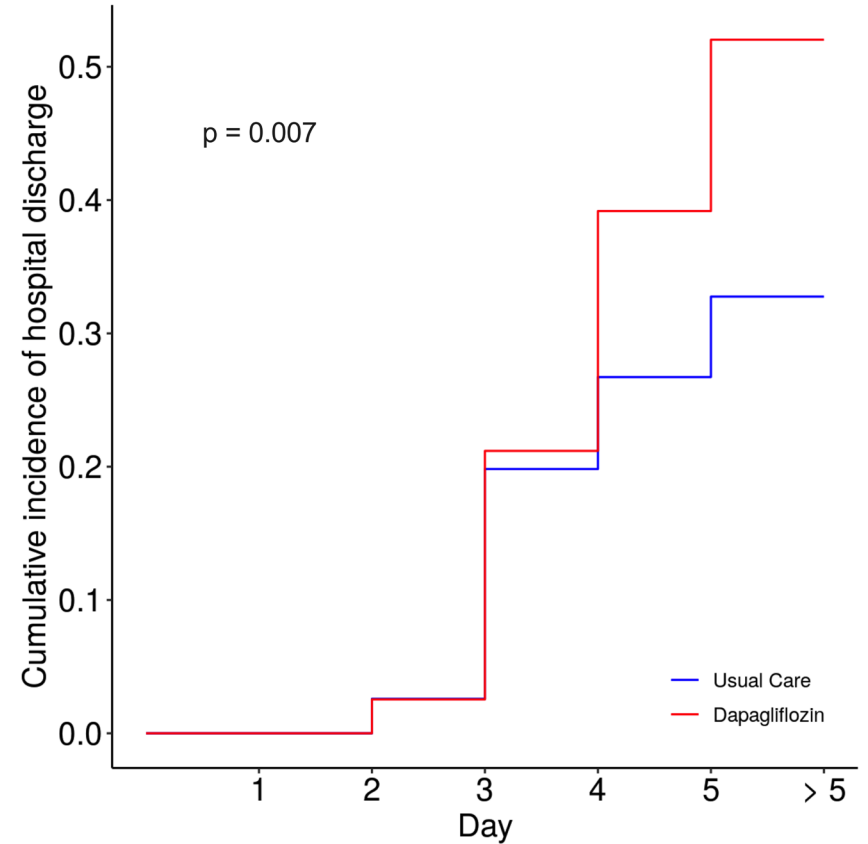
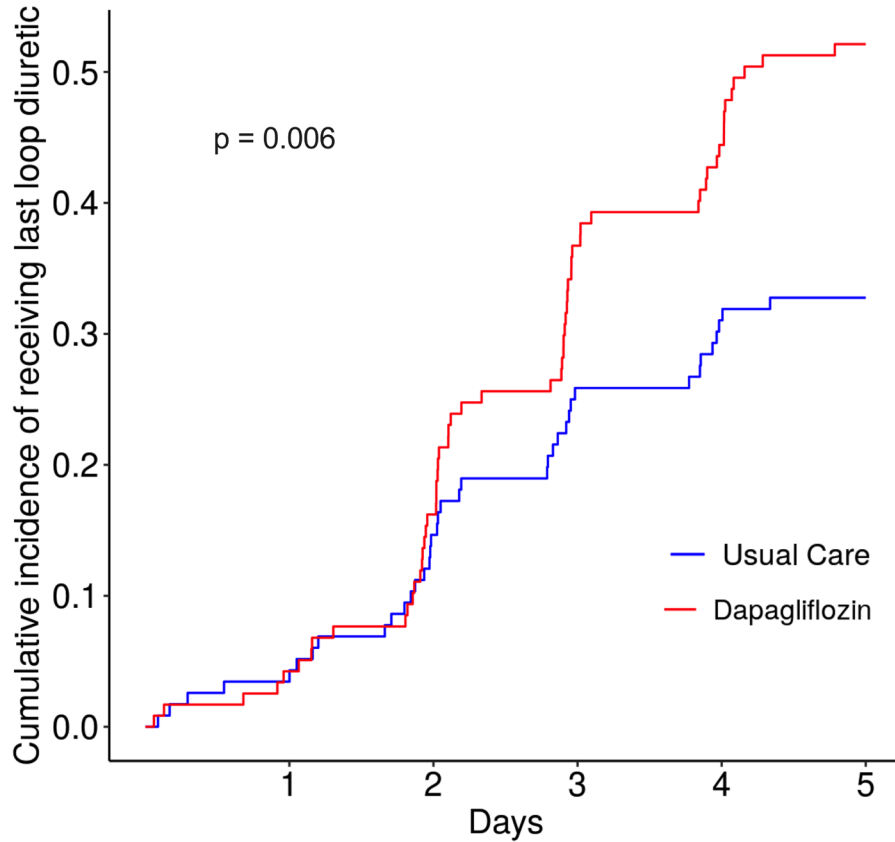
Improved 24-Hour Natriuresis with Dapagliflozin



Improved 24-Hour Diuresis with Dapagliflozin



Faster Time to Oral Diuretic Transition and Discharge



Secondary Outcomes

Secondary Outcomes, N	Usual Care	Dapagliflozin
Worsening heart failure	3	4
30-day hospital readmission for ADHF or diabetes-related reasons	8	7
ADHF-related readmission	8	6
Diabetes-related readmission	0	1

Safety Outcomes and Adverse Events

Safety Outcomes	Usual Care	Dapagliflozin
Ketoacidosis	0	0
Symptomatic hypotension	4	2
Prolonged hospitalization for hypotension	1	1
Hypoglycemia	9	7
Prolonged hospitalization for hypoglycemia	0	0
Genitourinary tract infections	1	0
Change in eGFR (mL/min/1.73m ²)	-3.0 (-9 to 2)	-2.0 (-10 to 4)

Conclusions

1. Dapagliflozin had a strong signal to improve diuretic efficiency supported by:
 - Increased natriuresis and diuresis per 40mg of IV furosemide
 - Decreased total dose and duration of loop diuretics required
 - Decreased time to hospital discharge
2. Early dapagliflozin initiation was safe across all diabetic and cardiorenal outcomes

Totality of DICTATE-AHF data supports the early initiation of dapagliflozin in AHF to safely facilitate decongestion and GDMT optimization

DICTATE-AHF Study Team

Principal Investigator: JoAnn Lindenfeld

Co- PI: Zachary Cox

Co- Investigator: Sean Collins

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