TIMI Study Group

DAPA ACT HF TIMI 68

Brigham and Women's Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

Effect of In-Hospital Initiation of Dapagliflozin on Decongestion in Patients Hospitalized for Heart Failure

A Prespecified Analysis of the DAPA ACT HF – TIMI 68 Trial

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for the DAPA ACT HF – TIMI 68 Investigators

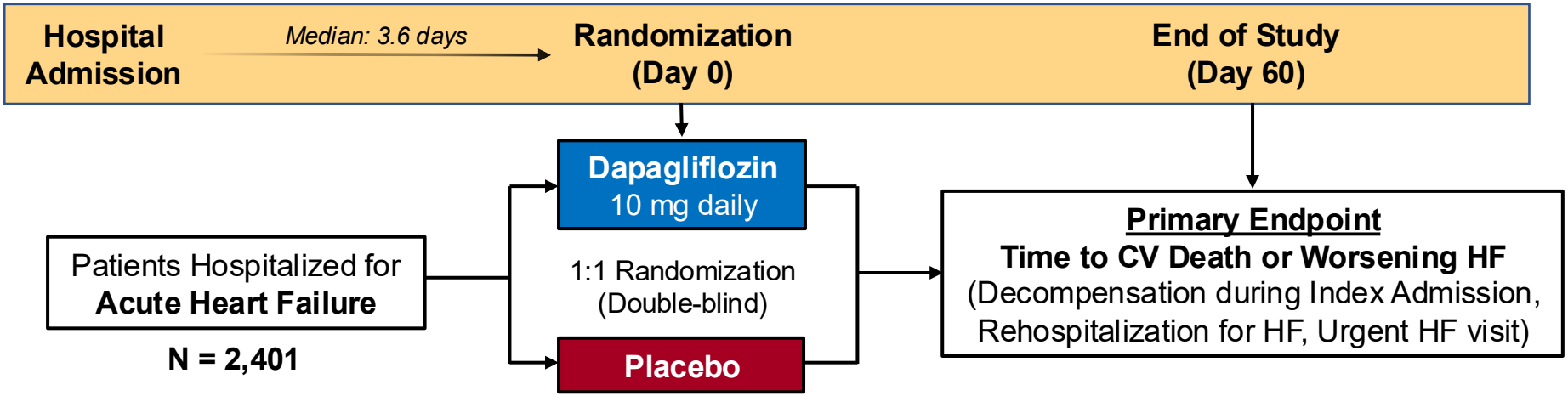
30 August 2026

Background

- Decongestion is a key therapeutic goal in patients hospitalized for HF
- Residual congestion at discharge is common and identifies patients at significantly higher risk for HF readmission and mortality in the vulnerable post-discharge period
- SGLT2 inhibitors may have favorable early effects on fluid balance through osmotic diuresis, natriuresis, and facilitation of interstitial drainage
- We sought to characterize the effects of dapagliflozin on multiple measures of congestion following in-hospital initiation

Bozkurt B, et al. *J Card Fail*. 2025;31:66-116.
Mentz RJ, et al. *Eur J Heart Fail*. 2014;16:471-482.

DAPA ACT HF – TIMI 68
Trial Design



Key Entry Criteria

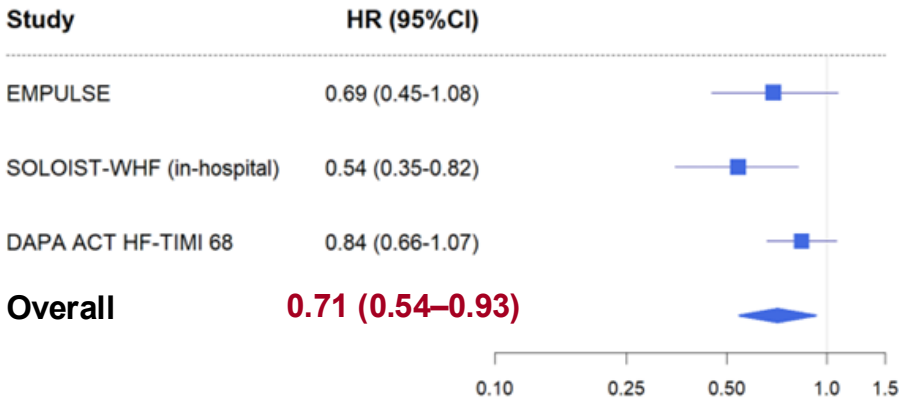
- Signs or symptoms of fluid overload
- Elevated NT-proBNP or BNP
- eGFR >25 ml/min/1.73 m^2
- Any LVEF, with or without T2D
- Newly diagnosed and worsening chronic HF
- >24 hr but <14 days after admission (early as possible)
- No intensification of IV diuretics for 12 hr, no IV vasoactives for 24 hr

Berg DD, et al. *Circulation*. 2025;152(20):1411–1422.
Berg DD, et al. *JACC Heart Fail*. 2025;13(5):829-839.

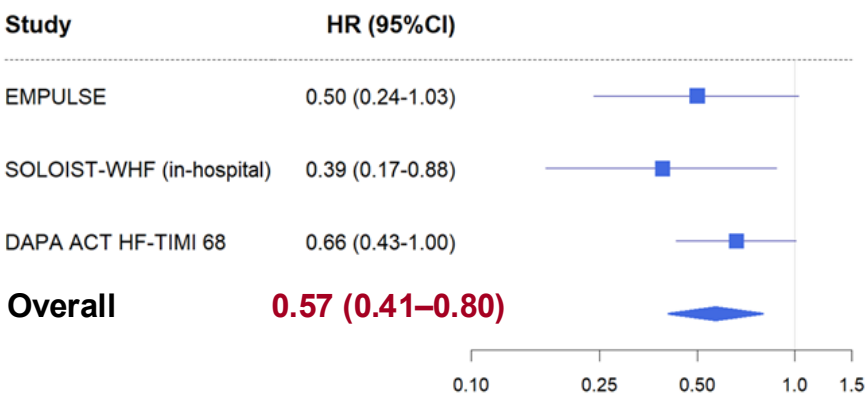
DAPA ACT HF – TIMI 68
Primary Results and Meta-Analysis

DAPA ACT HF
TIMI 68

Cardiovascular Death or Worsening HF Event



All-Cause Mortality



Totality of randomized trial data support early initiation of SGLT2i in patients hospitalized for HF to ↓ risk of adverse outcomes in early post-discharge period

Berg DD, et al. *Circulation*. 2025;152(20):1411–1422.

Congestion Endpoints

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- **Assessed at randomization, 1 week, 1 month, and 2 months**

- **Placebo-adjusted change in:**
  - Modified EVEREST Composite Congestion Score (CCS)
  - Body weight (kg)
  - Mean daily loop diuretic dose (furosemide 40 mg IV equivalent)
  - Diuretic efficiency (Δ in body weight per furosemide 40 mg IV equivalent)

Modified EVEREST CCS

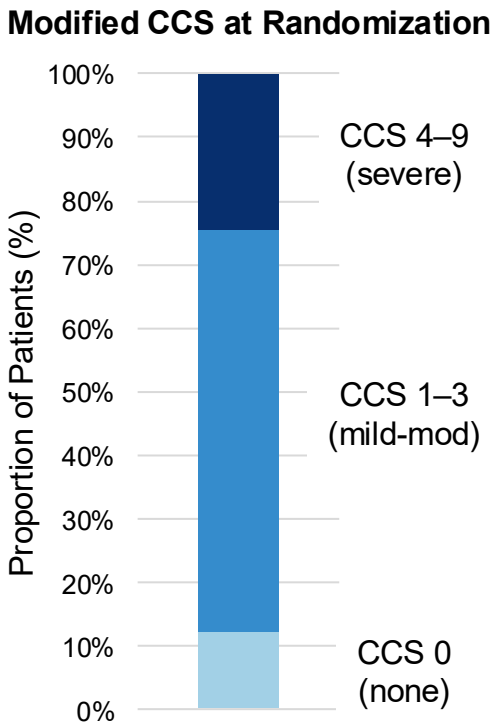
- **Six HF signs and symptoms assessed**
  - Fatigue, dyspnea, orthopnea, JVP, rales, and peripheral edema
  - Prospectively assessed at all study visits
  - Each graded 0–3 (0 = absent, 3 = severe)

- **Modified EVEREST CCS**
  - Orthopnea, JVP, and peripheral edema
  - Total score = 9 points

- ***Analyzed using linear MMRM model including all visits with evaluable CCS***

Konstam MA, et al. JAMA. 2007;297:1319–1331.

Baseline Characteristics



Characteristic	CCS 0 (N=205)	CCS 1–3 (N=1061)	CCS 4–9 (N=410)
Age (years)	68 (57, 76)	68 (58, 76)	66 (55, 74)
Female sex	65 (32)	354 (33)	115 (28)
Black race	33 (16)	191 (16)	125 (31)
Body-mass index (kg/m²)	28 (24, 33)	28 (25, 34)	31 (27, 39)
LVEF (%)	30 (21, 40)	30 (20, 45)	30 (20, 42)
Prior HF hospitalization	50/105 (48)	284/552 (51)	148/252 (59)
Type 2 diabetes mellitus	58 (28)	372 (35)	153 (37)
eGFR (ml/min/1.73 m²)	68 (51, 85)	65 (50, 83)	62 (46, 78)
KCCQ-TSS	40 (25, 60)	35 (21, 56)	25 (10, 38)
NT-proBNP (pg/ml)	4504 (2867, 9683)	4659 (2785, 8729)	5763 (3284, 9752)
BNP (pg/ml)	1053 (717, 1643)	1071 (704, 1852)	1215 (762, 2088)
*Z-score for combined NT-proBNP and BNP	–0.18 (–0.77, 0.61)	–0.14 (–0.79, 0.66)	0.09 (–0.59, 0.83)

*Z-score standardizes NT-proBNP and BNP to permit inclusion of patients with either qualifying biomarker

Prognostic Significance of CCS

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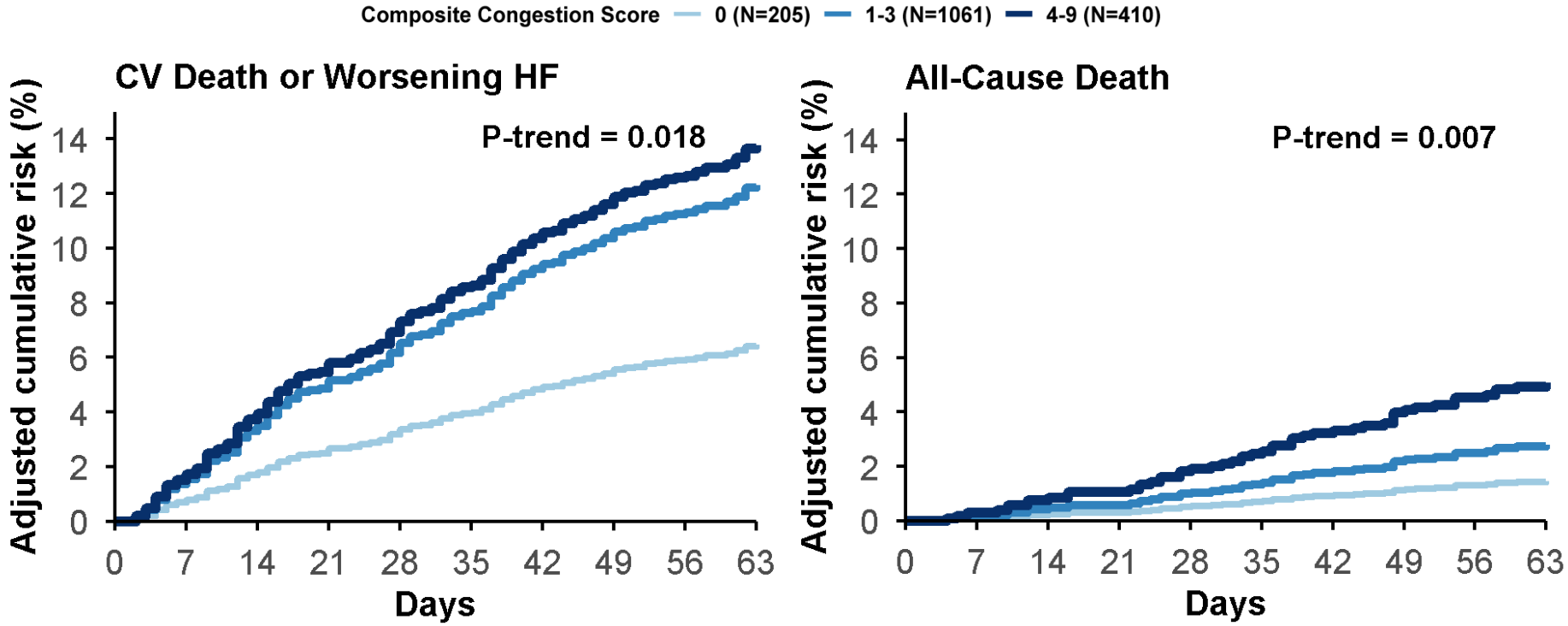

Models were adjusted for randomized treatment, age, eGFR, LVEF, prior HF hospitalization, prior stroke, AF, and use of noninvasive ventilation prior to randomization.

Prognostic Significance of CCS

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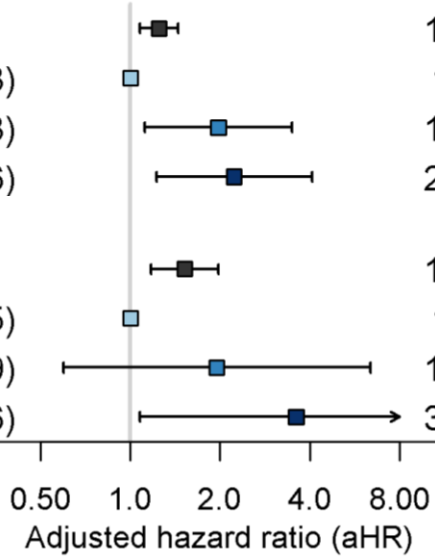
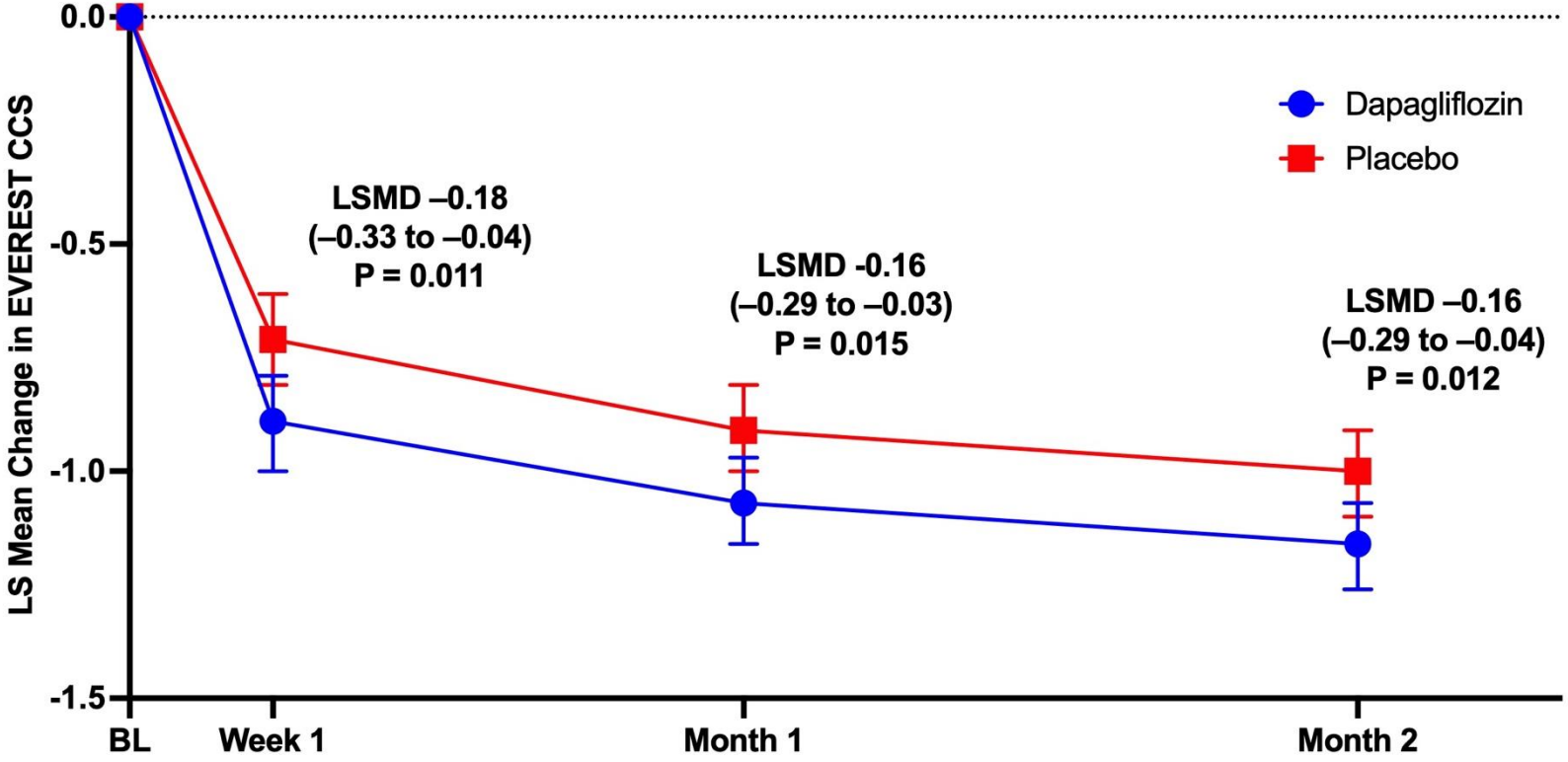
Outcome / Congestion Score	n/N (%)	aHR (95% CI)	P value
Primary composite outcome			
CCS (per 2-point increase)		1.25 (1.08–1.44)	0.003
0 (reference)	13 / 205 (6.3)	1.00 (reference)	
1-3	131 / 1061 (12.3)	1.97 (1.12–3.49)	
4-9	60 / 410 (14.6)	2.23 (1.22–4.07)	
All-cause death			
CCS (per 2-point increase)		1.52 (1.17–1.97)	0.002
0 (reference)	3 / 205 (1.5)	1.00 (reference)	
1-3	31 / 1061 (2.9)	1.95 (0.59–6.39)	
4-9	23 / 410 (5.6)	3.60 (1.08–12.0)	



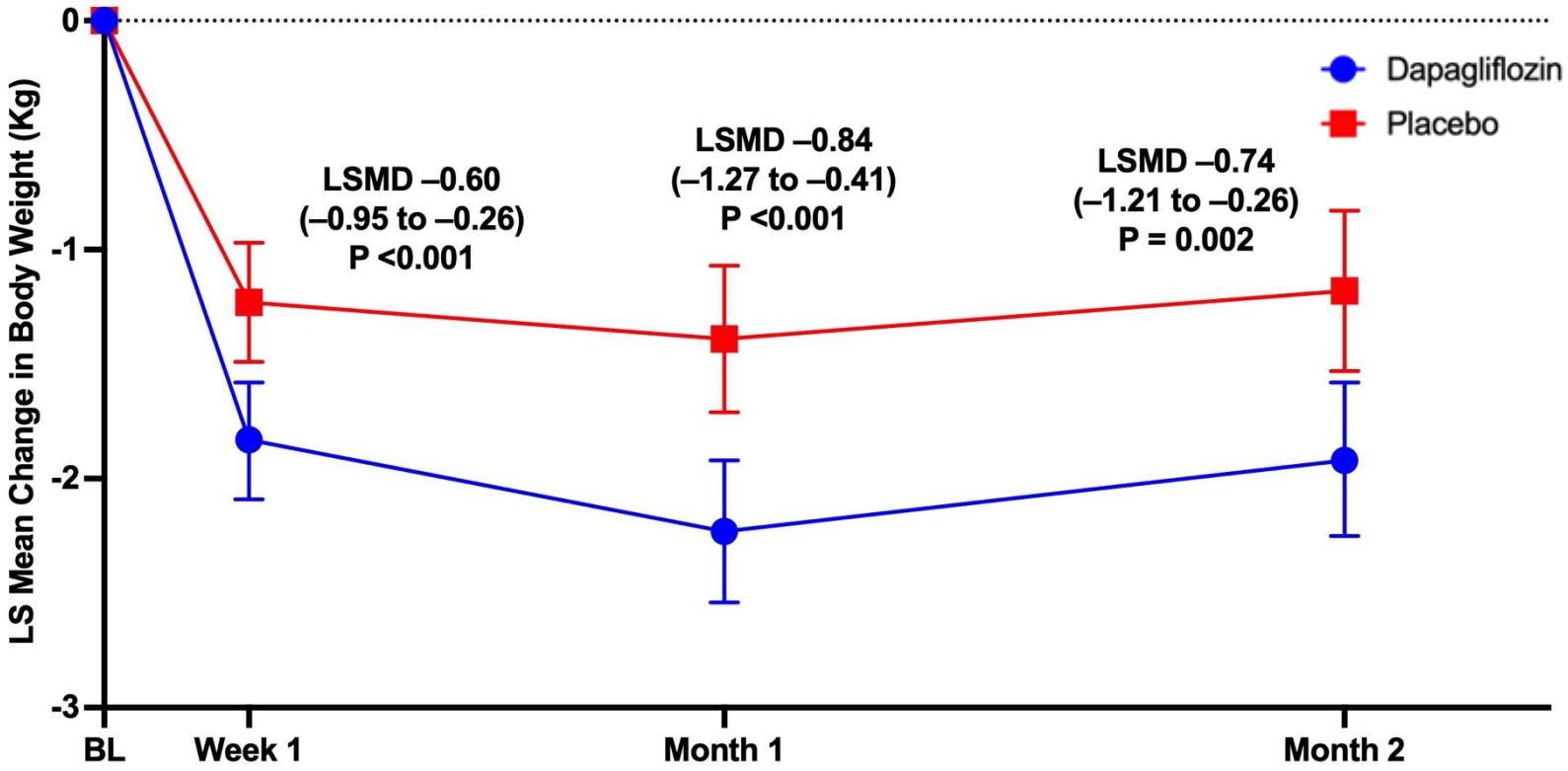
Models were adjusted for randomized treatment, age, eGFR, LVEF, prior HF hospitalization, prior stroke, AF, and use of noninvasive ventilation prior to randomization.

Modified EVEREST CCS



Results are presented as the least squares mean differences between treatment groups.
CI, confidence interval; LS, least squares; LSMD, least square mean difference.

Body Weight



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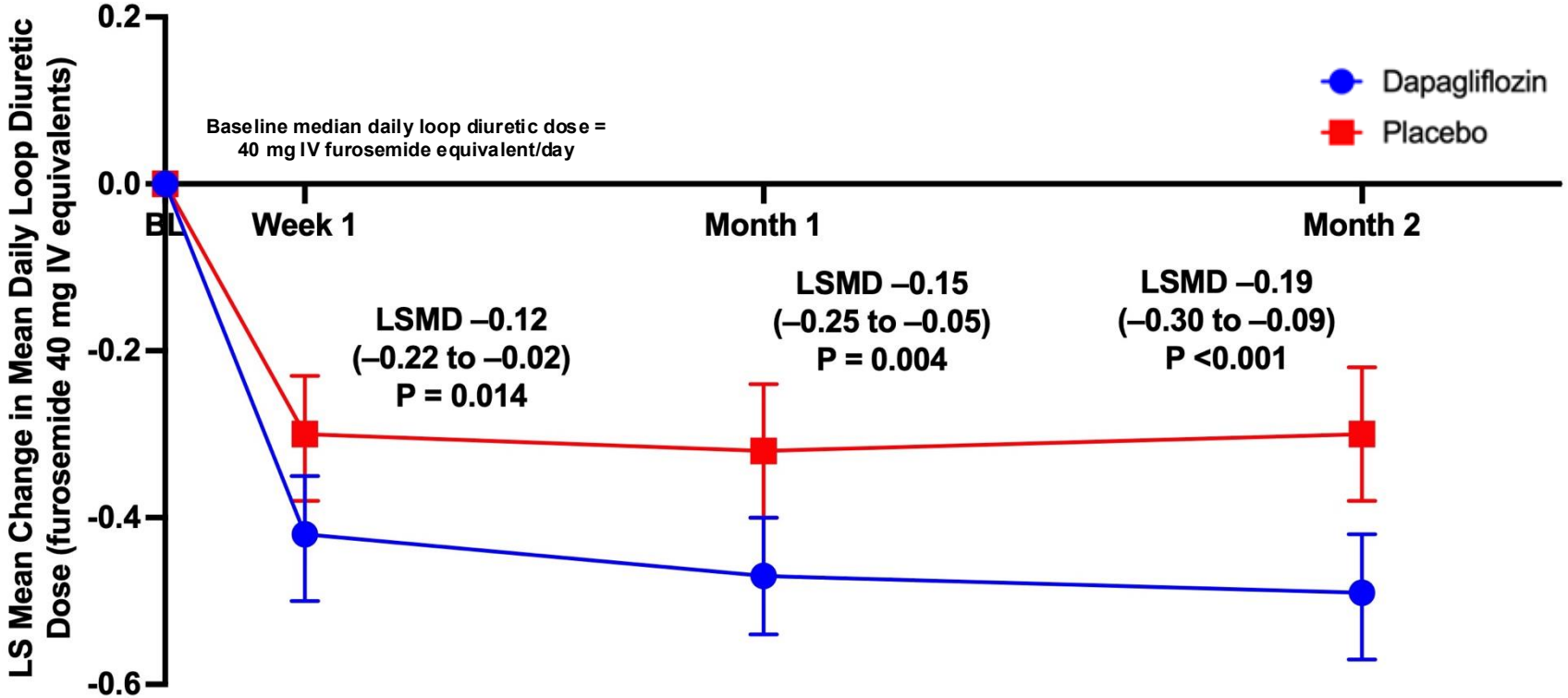
Mean Daily Loop Diuretic Dose



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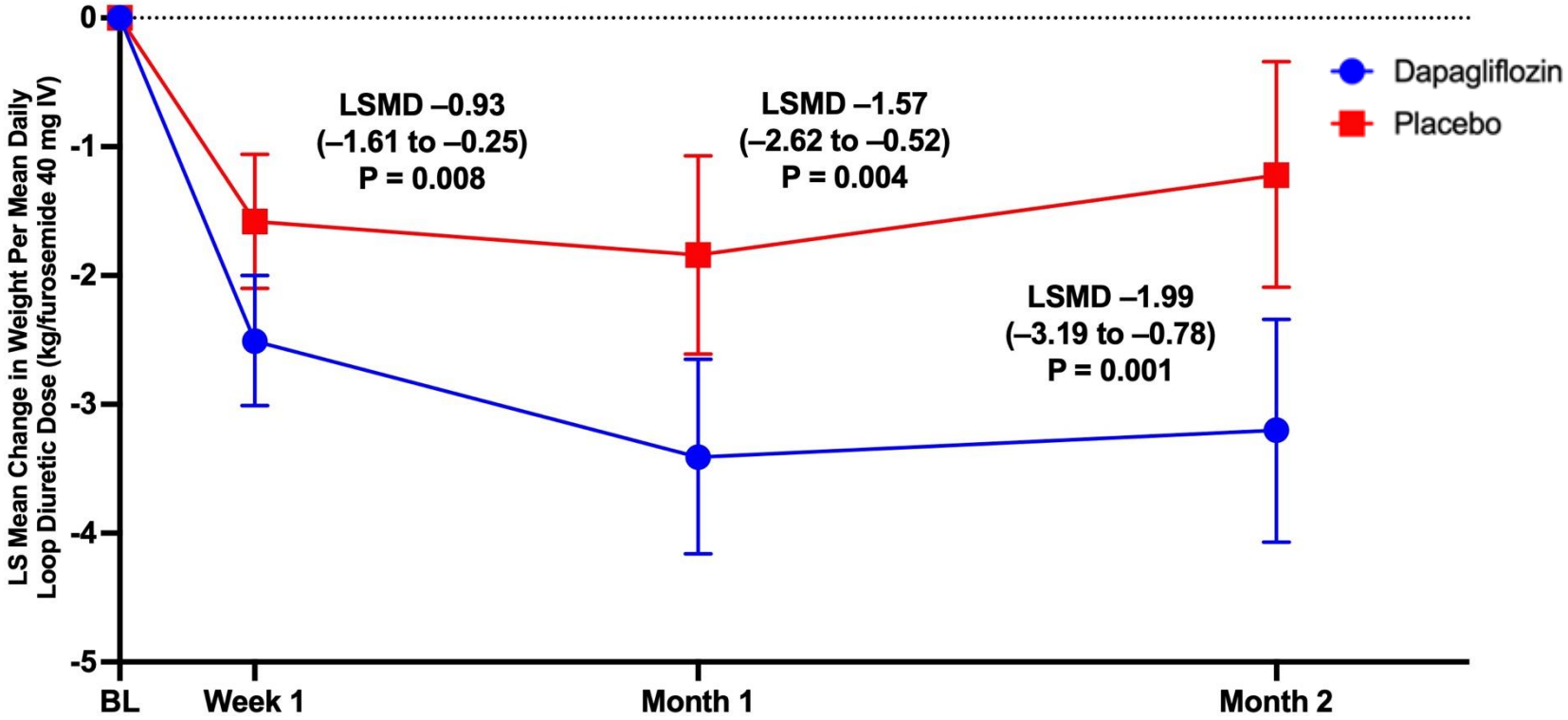
Diuretic Efficiency



Results are presented as the least squares mean differences between treatment groups.
CI, confidence interval; LS, least squares; LSMD, least square mean difference.

Limitations

- Clinical congestion assessment is subject to interobserver variability
- Some patients had missing congestion data
- Change in body weight is an imperfect surrogate for fluid loss in patients treated with SGLT2i
- Serial assessment of other measures of decongestion was not available

Conclusions

- Greater baseline congestion identified patients at higher risk of HF-related events and death in the early post-discharge period
- In-hospital initiation of dapagliflozin led to improvements across multiple measures of congestion within 1 week that were sustained through 2 months
- Diuretic efficiency progressively improved over time, reflecting sustained weight loss with lower background loop diuretic requirements

Simultaneously Published in *JACC: Heart Failure*

JACC: HEART FAILURE VOL. ■, NO. ■, 2026

ORIGINAL RESEARCH

Effect of In-Hospital Initiation of Dapagliflozin on Decongestion in Patients Hospitalized for Heart Failure

An Analysis of the DAPA ACT HF-TIMI 68 Trial

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ABSTRACT

BACKGROUND Safe and effective decongestion remains an important therapeutic goal in patients hospitalized for heart failure.

OBJECTIVES The authors evaluated the effect of dapagliflozin on multiple clinically relevant measures of congestion among patients hospitalized for heart failure.

METHODS This was a prespecified analysis of DAPA ACT HF-TIMI 68 (Dapagliflozin Effect on Cardiovascular Events in Acute Heart Failure–Thrombolysis in Myocardial Infarction 68), a randomized, placebo-controlled trial evaluating in-hospital initiation of dapagliflozin on clinical outcomes through 2 months. The authors assessed placebo-adjusted changes from baseline in modified EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure) Composite Congestion Score (CCS), body weight, mean daily loop diuretic dose (furosemide 40 mg intravenous [IV] equivalents), and body weight adjusted for mean daily loop diuretic dose (diuretic efficiency) at 1 week, 1 month, and 2 months using linear mixed-effects models for repeated measures.

RESULTS At randomization, 12%, 63%, and 24% had no congestion (CCS 0), mild-to-moderate congestion (CCS 1-3), and severe congestion (CCS 4-9), respectively. Compared with placebo, dapagliflozin improved all decongestion-related endpoints by 1 week, including CCS (least squares mean difference [LSMD]: −0.18; 95% CI: −0.33 to −0.04; $P = 0.011$), body weight (LSMD: −0.60 kg; 95% CI: −0.95 to −0.26; $P < 0.001$), mean daily loop diuretic dose (LSMD: −0.12 furosemide 40-mg IV equivalents; 95% CI: −0.22 to −0.02; $P = 0.014$), and diuretic efficiency (LSMD: −0.93 kg/furosemide 40 mg IV equivalents; 95% CI: −1.61 to −0.25; $P = 0.008$). These improvements were sustained through 2 months, with progressive increases in diuretic efficiency through 2 months (LSMD: −1.99 kg/furosemide 40 mg IV equivalents; 95% CI: −3.19 to −0.78; $P < 0.001$).

CONCLUSIONS In-hospital initiation of dapagliflozin led to modest but significant improvements across multiple measures of congestion within 1 week that were sustained through 2 months. Diuretic efficiency progressively improved through 2 months. (Dapagliflozin Effect on Cardiovascular Events in Acute Heart Failure–Thrombolysis in Myocardial Infarction 68 [DAPA ACT HF-TIMI 68]; NCT04363697) (JACC Heart Fail. 2026;■:103366) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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JACC Heart Failure