

Effect of dapagliflozin on outpatient worsening of patients with heart failure and reduced ejection fraction: A prespecified analysis of DAPA-HF.

SUPPLEMENTAL MATERIAL

Supplemental Table I: Risk of death from any cause after a hospitalization for heart failure, urgent heart failure visit, and intensification of therapy for heart failure using a cox model with event type as the first event experienced.

	No Event	Hospitalization for HF	Urgent HF Visit	Intensification of HF Therapy
Each event as the first event experienced in a time-updated model, hazard ratio (95% CI)				
Adjusted for randomized treatment and prior HF hospitalization	1	8.36 (6.89-10.15)	7.04 (3.32-14.90)	3.12 (2.38-4.09)
Adjusted for randomized treatment , prior HF hospitalization and baseline covariates*	1	6.21 (5.07-7.62)	3.00 (1.39-6.48)	2.67 (2.03-3.52)

All models stratified by diabetes status.

*Adjusted for randomized treatment, age, sex, region, race, NYHA functional classification, left ventricular ejection fraction, body mass index, pulse, systolic blood pressure, serum creatinine, log NT-proBNP, history of previous HF hospitalization, atrial fibrillation, stroke, myocardial infarction, hypertension , ischemic etiology and use of implantable cardioverter defibrillator and/or cardiac resynchronization therapy.

Supplemental Table II: Risk of death from any cause after a hospitalization for heart failure, urgent heart failure visit, and intensification of therapy for heart failure using a cox model with event type as the first event experienced – sensitivity analysis limiting the definition of outpatient HF worsening events to include only those in which the dose of diuretics was increased and sustained for at least four weeks.

	No Event	Hospitalization for HF	Urgent HF Visit	Intensification of HF Therapy (diuretics only)
Each event as the first event experienced in a time-updated model, hazard ratio (95% CI)				
Unadjusted	1	8.53 (7.06-10.30)	6.50 (3.07-13.75)	3.38 (2.54-4.49)
Adjusted for randomized treatment and prior HF hospitalization	1	8.26 (6.81-10.00)	6.30 (2.97-13.34)	3.37 (2.53-4.48)
Adjusted for randomized treatment , prior HF hospitalization and baseline covariates*	1	6.14 (5.01-7.51)	2.85 (1.32-6.14)	2.82 (2.11-3.77)

All adjusted models stratified by diabetes status.

*Adjusted for randomized treatment, age, sex, region, race, NYHA functional classification, left ventricular ejection fraction, body mass index, pulse, systolic blood pressure, serum creatinine, log NT-proBNP, history of previous HF hospitalization, atrial fibrillation, stroke, myocardial infarction, hypertension , ischemic etiology and use of implantable cardioverter defibrillator and/or cardiac resynchronization therapy.

Supplemental Table III: Risk of death from any cause after a hospitalization for heart failure, urgent heart failure visit, and intensification of therapy for heart failure using a cox model with event type as the first event experienced – sensitivity analysis using a 7-day period between events to identify independent events

	No Event	Hospitalization for HF	Urgent HF Visit	Intensification of HF Therapy (diuretics only)
Each event as the first event experienced in a time-updated model, hazard ratio (95% CI)				
Unadjusted	1	8.32 (6.86-10.09)	7.07 (3.34-14.96)	3.52 (2.72-4.54)
Adjusted for randomized treatment and prior HF hospitalization	1	8.03 (6.60-9.78)	6.84 (3.23-14.49)	3.50 (2.70-4.52)
Adjusted for randomized treatment , prior HF hospitalization and baseline covariates*	1	5.96 (4.85-7.33)	3.04 (1.41-6.59)	2.96 (2.28-3.84)

All adjusted models stratified by diabetes status.

*Adjusted for randomized treatment, age, sex, region, race, NYHA functional classification, left ventricular ejection fraction, body mass index, pulse, systolic blood pressure, serum creatinine, log NT-proBNP, history of previous HF hospitalization, atrial fibrillation, stroke, myocardial infarction, hypertension , ischemic etiology and use of implantable cardioverter defibrillator and/or cardiac resynchronization therapy.