Supplemental Material

Table of Contents

eTABLE 1. Baseline Characteristics of Participants included in the Electronic Health Record (EHR) Ancillary Study versus Remaining Trial Participants at EHR Ancillary Study Sites

Characteristic	EHR Ancillary Study N=3644	Not in EHR Ancillary Study N=1818	P value
Randomized to intensive treatment, No. (%)	1849 (50.7)	883 (48.6)	0.14
Age, yr			
Mean ± SD	68.9 ± 9.3	67.3 ± 9.6	<0.001
≥75, n (%)	1158 (31.8)	453 (24.9)	<0.001
Female sex, n (%)	877 (24.1)	709 (39.0)	<0.001
Race/Ethnicity, n (%)			<0.001
White	2341 (64.2)	1018 (56.0)	
Black	1109 (30.4)	652 (35.9)	
Hispanic	149 (4.1)	105 (5.8)	
Other	45 (1.2)	43 (2.4)	
Smoking status, n (%)			<0.001
Current smoker	476 (13.1)	277 (15.2)	
Former smoker	1776 (48.7)	733 (40.3)	
Never smoker	1392 (38.2)	808 (44.4)	
BMI, mean ± SD, kg/m^2	30.0 (5.7)	29.7 (5.6)	0.03
History of cardiovascular disease, n (%)	881 (24.2)	324 (17.8)	<0.001
Blood pressure, mean ± SD, mm Hg			
Systolic	137.7 ± 15.0	140.0 ± 16.6	<0.001
Diastolic	76.9 ± 11.5	78.5 ± 12.3	<0.001
Orthostatic hypotension, n (%)	244 (6.7)	124 (6.9)	0.90
eGFR, ml/min/1.73 m^2			
Mean ± SD	71.1 ± 19.5	74.3 ± 18.7	<0.001
<60, No. (%)	1066 (29.3)	413 (22.9)	<0.001
Urine albumin to creatinine ratio, median [IQR], mg/g	9.8 [5.7 to 24.2]	9.2 [5.6, 20.0]	0.02
HDL cholesterol, mean ± SD, mg/dL	51.5 ± 13.8	53.5 ± 14.9	<0.001
Triglycerides, median [IQR], mg/dL	108 [78 to 150]	100 [73 to 142]	<0.001
Glucose, mean ± SD, mg/dL	99.5 ± 13.3	99.0 ± 14.4	0.25
No. of antihypertensive agents, mean ± SD	1.9 ± 1.0	1.8 ± 1.1	<0.001
Statin use, n (%)	1856 (50.9)	708 (38.9)	<0.001
Use of ACE inhibitor or Angiotensin receptor blocker, n (%)	2125 (58.3)	1024 (56.3)	0.17

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index; eGFR, estimated glomerular filtration rate based on the 2021 CKD-EPI creatinine equation; HDL, high-density lipoprotein; IQR, interquartile range; SD, standard deviation.

eTABLE 2. Stage of outpatient and inpatient acute kidney injury events by treatment group

	Intensive Treatment Events (%)	Standard Treatment Events (%)	
Outpatient AKI (creatinine-based)			
	Intensive Treatment Events (%)	Standard Treatment Events (%)	P value=0.73
AKI stage 1	208 (85.6%)	152 (87.9%)	
AKI stage 2	29 (11.9%)	16 (9.2%)	
AKI stage 3	6 (2.5%)	5 (2.9%)	
Inpatient AKI (creatinine-based)			
	Intensive Treatment Events (%)	Standard Treatment Events (%)	P value=0.05
AKI stage 1	146 (78.1%)	129 (83.2%)	
AKI stage 2	31 (16.6%)	13 (8.4%)	
AKI stage 3	10 (5.3%)	13 (8.4%)	

AKI, acute kidney injury. AKI stage 1 = serum creatinine ≥0.3 mg/dl or 1.5 to <2.0 times baseline serum creatinine, AKI stage 2 = ≥2.0 but <3.0 times baseline, and AKI stage 3 = ≥3.0 times baseline. Stage 1 outpatient AKI did not include those with only a ≥0.3 mg/dl increase. P values based on Fisher's exact test comparing distribution of AKI severity by treatment group.

eTABLE 3. Effect of intensive treatment on the incidence of acute kidney injury accounting for the competing risk of mortality

Population	Outcome	Intensive Events / Cum Inc at 3.8 Yrs	Standard Events / Cum Inc at 3.8 Yrs	Hazard Ratio (95% CI)	P value
All participants (N=9361)	Inpatient AKI based on SAE	179 / 3.8%	109 / 2.4%	1.69 (1.30, 2.20)	<0.001
EHR Ancillary Study (N=3644)	Inpatient AKI based on SAE	95 / 5.2%	61 / 3.4%	1.57 (1.13, 2.19)	0.007
EHR Ancillary Study (N=3644)	Outpatient AKI (Trial+EHR Labs)	243 / 12.4%	173 / 8.9%	1.48 (1.20, 1.82)	<0.001
EHR Ancillary Study (N=3644)	Outpatient AKI (Trial Labs Only)	130 / 6.9%	78 / 4.4%	1.66 (1.28, 2.16)	<0.001
EHR Ancillary Study (N=3644)	Inpatient AKI (EHR Labs)	187 / 9.6%	155 / 8.1%	1.15 (0.91, 1.46)	0.24

CI, confidence interval; Cum Inc, cumulative incidence; EHR, electronic health record, SCr: serum creatinine. Hazard ratio based on the Fine-Gray subdistribution hazard model accounting for the competing risk of death.