

**Finerenone in Patients With Chronic Kidney Disease and
Type 2 Diabetes According to Baseline HbA_{1c}: An Analysis**

From the FIDELIO-DKD Study

Online-Only Supplemental Material

Supplementary Table 1—Patients initiating insulin or insulin analogs during the study

Baseline	Initiated insulin postbaseline*	Finerenone (<i>n</i> = 2,833)	Placebo (<i>n</i> = 2,841)	Total (<i>N</i> = 5,674)
Yes (<i>n</i> = 3,637)	Yes	0	0	0
	No	1,843 (65.1)	1,794 (63.1)	3,637 (64.1)
No (<i>n</i> = 2,037)	Yes	209 (7.4)	260 (9.2)	469 (8.3)
	No	781 (27.6)	787 (27.7)	1,568 (27.6)

Data are presented as n (%).

*At any time during the trial.

Supplementary Table 2—Overall safety and treatment-emergent hyperkalemia-related events in patients according to baseline insulin use

<i>n</i> (%)	Baseline insulin use			
	Without insulin use		With insulin use	
	Finerenone (<i>n</i> = 989)	Placebo (<i>n</i> = 1,041)	Finerenone (<i>n</i> = 1,838)	Placebo (<i>n</i> = 1,790)
Any investigator-reported AE	854 (86.3)	903 (86.7)	1,614 (87.8)	1,575 (88.0)
Related to study drug	205 (20.7)	148 (14.2)	441 (24.0)	301 (16.8)
Leading to discontinuation	76 (7.7)	69 (6.6)	131 (7.1)	99 (5.5)
Any SAE	282 (28.5)	318 (30.5)	620 (33.7)	653 (36.5)
Related to study drug	12 (1.2)	11 (1.1)	36 (2.0)	23 (1.3)
Leading to discontinuation	26 (2.6)	33 (3.2)	49 (2.7)	45 (2.5)
AE with outcome death	7 (0.7)	15 (1.4)	24 (1.3)	36 (2.0)
Investigator-reported hyperkalemia-related AEs*				
Any AE	157 (15.9)	80 (7.7)	359 (19.5)	175 (9.8)
Related to study drug	96 (9.7)	36 (3.5)	237 (12.9)	99 (5.5)
Leading to discontinuation	19 (1.9)	6 (0.6)	45 (2.4)	19 (1.1)
Any SAE	15 (1.5)	2 (0.2)	29 (1.6)	10 (0.6)
Related to study drug	7 (0.7)	1 (<0.1)	19 (1.0)	4 (0.2)
Leading to hospitalization	13 (1.3)	2 (0.2)	27 (1.5)	6 (0.3)
Central laboratory assessment of serum potassium levels[†]				
>5.5 mmol/L	213/989 (21.5)	85/1,041 (8.2)	400/1,835 (21.8)	191/1,788 (10.7)
>6.0 mmol/L	45/989 (4.6)	13/1,041 (1.2)	82/1,835 (4.5)	27/1,788 (1.5)

*Reported using the MedDRA-preferred terms “hyperkalemia” and “blood potassium

increased”; [†]Data are from the full analysis set, not the safety analysis set.

AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event.

**Supplementary Table 3—Treatment-emergent adverse events affecting >5% of patients
in any treatment group by HbA_{1c} at baseline**

<i>n</i> (%)	Baseline HbA _{1c}			
	HbA _{1c} <7.5%		HbA _{1c} ≥7.5%	
	Finerenone (<i>n</i> = 1,382)	Placebo (<i>n</i> = 1,407)	Finerenone (<i>n</i> = 1,439)	Placebo (<i>n</i> = 1,421)
Hyperkalemia	224 (16.2)	107 (7.6)	221 (15.4)	114 (8.0)
Peripheral edema	82 (5.9)	140 (10.0)	104 (7.2)	164 (11.5)
Nasopharyngitis	121 (8.8)	141 (10.0)	120 (8.3)	109 (7.7)
Hypertension	102 (7.4)	132 (9.4)	110 (7.6)	141 (9.9)
Hypoglycemia	69 (5.0)	77 (5.5)	82 (5.7)	117 (8.2)
Urinary tract infection	83 (6.0)	78 (5.5)	96 (6.7)	114 (8.0)
Upper respiratory tract infection	95 (6.9)	108 (7.7)	86 (6.0)	81 (5.7)
Anemia	102 (7.4)	105 (7.5)	107 (7.4)	86 (6.1)
Diarrhea	86 (6.2)	93 (6.6)	98 (6.8)	96 (6.8)
Glomerular filtration rate decreased	84 (6.1)	70 (5.0)	95 (6.6)	62 (4.4)
Back pain	90 (6.5)	87 (6.2)	85 (5.9)	88 (6.2)
Constipation	72 (5.2)	72 (5.1)	59 (4.1)	91 (6.4)
Pneumonia	53 (3.8)	90 (6.4)	75 (5.2)	91 (6.4)
Dizziness	65 (4.7)	65 (4.6)	81 (5.6)	88 (6.2)
Bronchitis	59 (4.3)	74 (5.3)	75 (5.2)	77 (5.4)
Arthralgia	67 (4.8)	75 (5.3)	75 (5.2)	74 (5.2)
Pain in extremity	47 (3.4)	30 (2.1)	57 (4.0)	76 (5.3)
Acute kidney injury	53 (3.8)	62 (4.4)	76 (5.3)	74 (5.2)
Cough	49 (3.5)	53 (3.8)	61 (4.2)	74 (5.2)
Hypotension	72 (5.2)	42 (3.0)	54 (3.8)	45 (3.2)

**Supplementary Table 4—Treatment-emergent adverse events affecting >5% of patients
in any treatment group by insulin use at baseline**

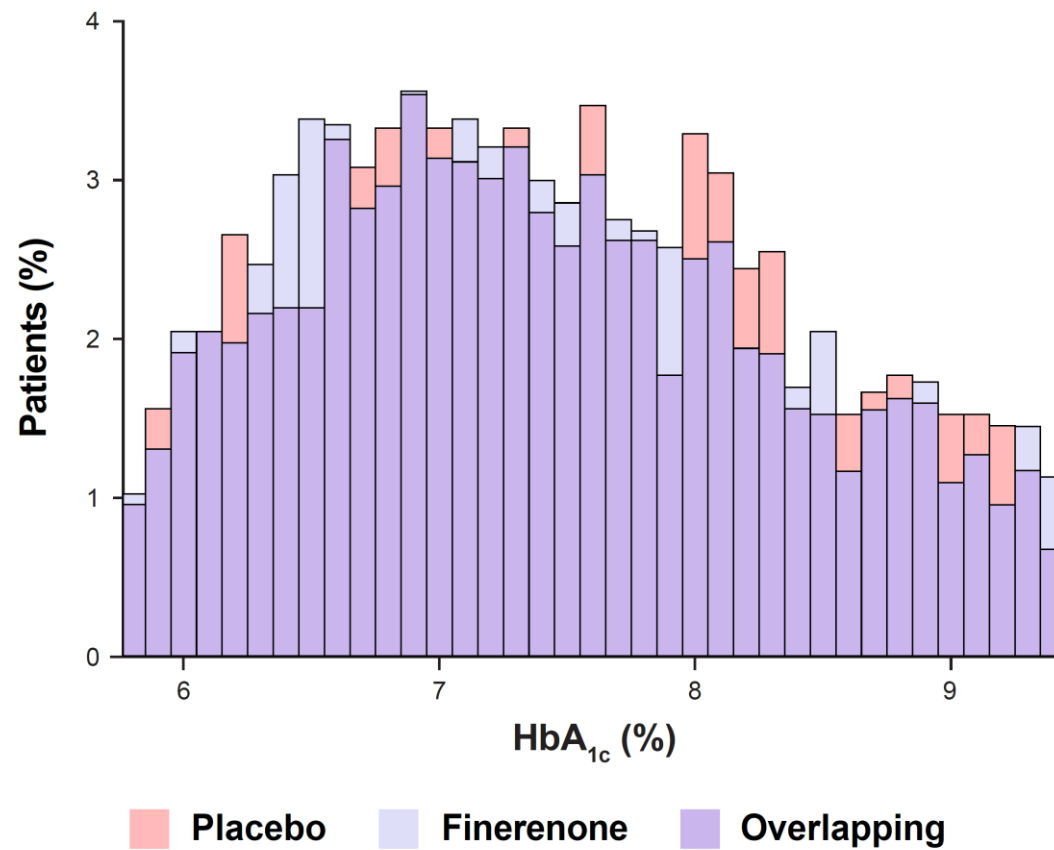
<i>n</i> (%)	Baseline insulin use			
	Without insulin		With insulin	
	Finerenone (<i>n</i> = 989)	Placebo (<i>n</i> = 1,041)	Finerenone (<i>n</i> = 1,838)	Placebo (<i>n</i> = 1,790)
Hyperkalemia	133 (13.4)	67 (6.4)	313 (17.0)	154 (8.6)
Peripheral edema	47 (4.8)	87 (8.4)	139 (7.6)	217 (12.1)
Nasopharyngitis	106 (10.7)	119 (11.4)	135 (7.3)	131 (7.3)
Hypertension	67 (6.8)	97 (9.3)	145 (7.9)	176 (9.8)
Hypoglycemia	30 (3.0)	29 (2.8)	121 (6.6)	165 (9.2)
Urinary tract infection	49 (5.0)	52 (5.0)	130 (7.1)	140 (7.8)
Anemia	74 (7.5)	74 (7.1)	135 (7.3)	117 (6.5)
Upper respiratory tract infection	55 (5.6)	56 (5.4)	126 (6.9)	133 (7.4)
Pneumonia	31 (3.1)	51 (4.9)	97 (5.3)	130 (7.3)
Diarrhea	63 (6.4)	68 (6.5)	121 (6.6)	121 (6.8)
Glomerular filtration rate decreased	54 (5.5)	44 (4.2)	125 (6.8)	89 (5.0)
Back pain	63 (6.4)	54 (5.2)	112 (6.1)	121 (6.8)
Constipation	50 (5.1)	52 (5.0)	81 (4.4)	111 (6.2)
Dizziness	40 (4.0)	47 (4.5)	106 (5.8)	106 (5.9)
Arthralgia	48 (4.9)	51 (4.9)	94 (5.1)	98 (5.5)
Bronchitis	42 (4.2)	53 (5.1)	92 (5.0)	98 (5.5)

Supplementary Table 5—Treatment-emergent serious adverse events affecting ≥1% of patients in any treatment group by HbA_{1c} at baseline

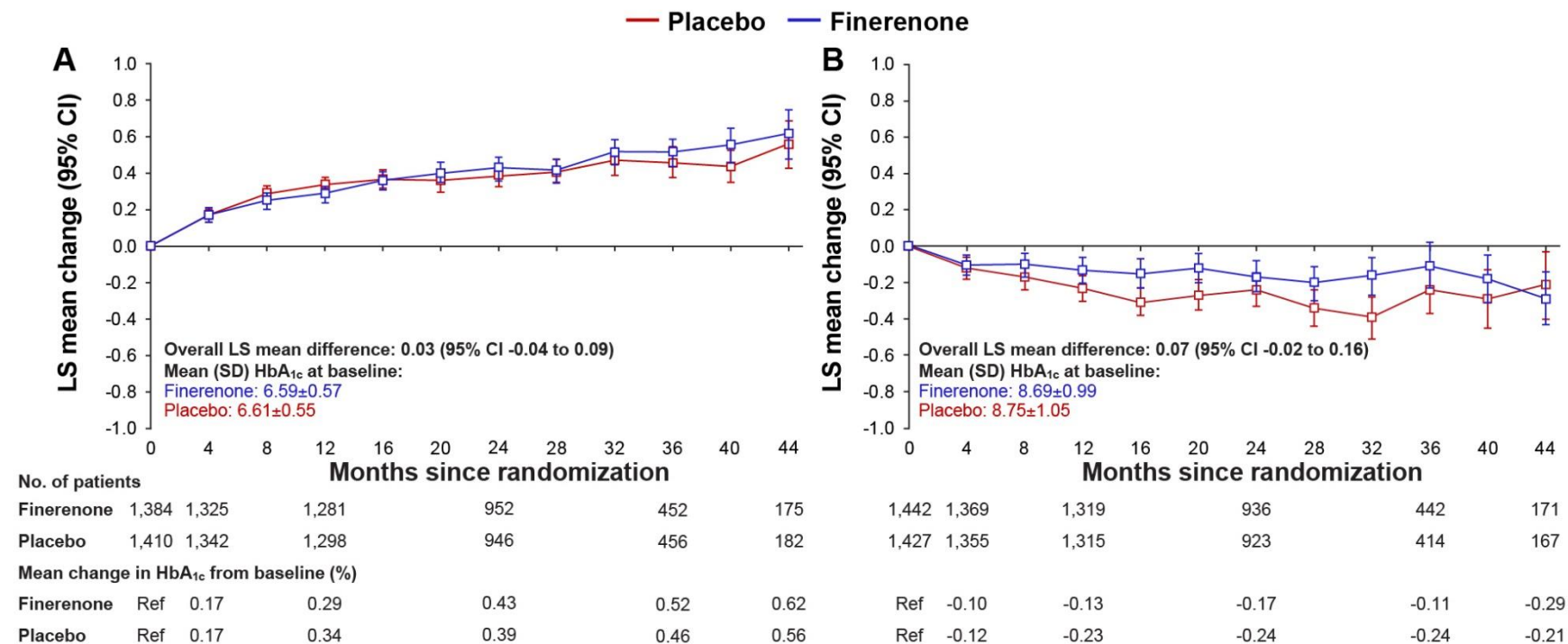
<i>n</i> (%)	Baseline HbA _{1c}			
	HbA _{1c} <7.5%		HbA _{1c} ≥7.5%	
	Finerenone (<i>n</i> = 1,382)	Placebo (<i>n</i> = 1,407)	Finerenone (<i>n</i> = 1,439)	Placebo (<i>n</i> = 1,421)
Pneumonia	27 (2.0)	54 (3.8)	43 (3.0)	49 (3.4)
Acute kidney injury	24 (1.7)	25 (1.8)	32 (2.2)	26 (1.8)
Hyperkalemia	21 (1.5)	2 (0.1)	20 (1.4)	10 (0.7)
Cellulitis	6 (0.4)	7 (0.5)	20 (1.4)	15 (1.1)
Hypoglycemia	10 (0.7)	12 (0.9)	11 (0.8)	19 (1.3)
Hyperglycemia	6 (0.4)	5 (0.4)	11 (0.8)	18 (1.3)
Urinary tract infection	6 (0.4)	6 (0.4)	15 (1.0)	17 (1.2)
Diabetes mellitus inadequate control	4 (0.3)	2 (0.1)	8 (0.6)	17 (1.2)
Syncope	6 (0.4)	6 (0.4)	6 (0.4)	16 (1.1)
Hypertension	7 (0.5)	14 (1.0)	8 (0.6)	9 (0.6)

Supplementary Table 6—Treatment-emergent serious adverse events affecting ≥1% of patients in any treatment group by insulin use at baseline

<i>n</i> (%)	Baseline insulin use			
	Without insulin		With insulin	
	Finerenone (<i>n</i> = 989)	Placebo (<i>n</i> = 1,041)	Finerenone (<i>n</i> = 1,838)	Placebo (<i>n</i> = 1,790)
Pneumonia	16 (1.6)	30 (2.9)	54 (2.9)	73 (4.1)
Acute kidney injury	17 (1.7)	19 (1.8)	39 (2.1)	32 (1.8)
Hyperkalemia	15 (1.5)	2 (0.2)	27 (1.5)	10 (0.6)
Hypoglycemia	7 (0.7)	5 (0.5)	14 (0.8)	26 (1.5)
Cellulitis	4 (0.4)	7 (0.7)	22 (1.2)	15 (0.8)
Hyperglycemia	4 (0.4)	4 (0.4)	13 (0.7)	19 (1.1)
Urinary tract infection	3 (0.3)	5 (0.5)	18 (1.0)	18 (1.0)
Type 2 diabetes	2 (0.2)	4 (0.4)	12 (0.7)	18 (1.0)

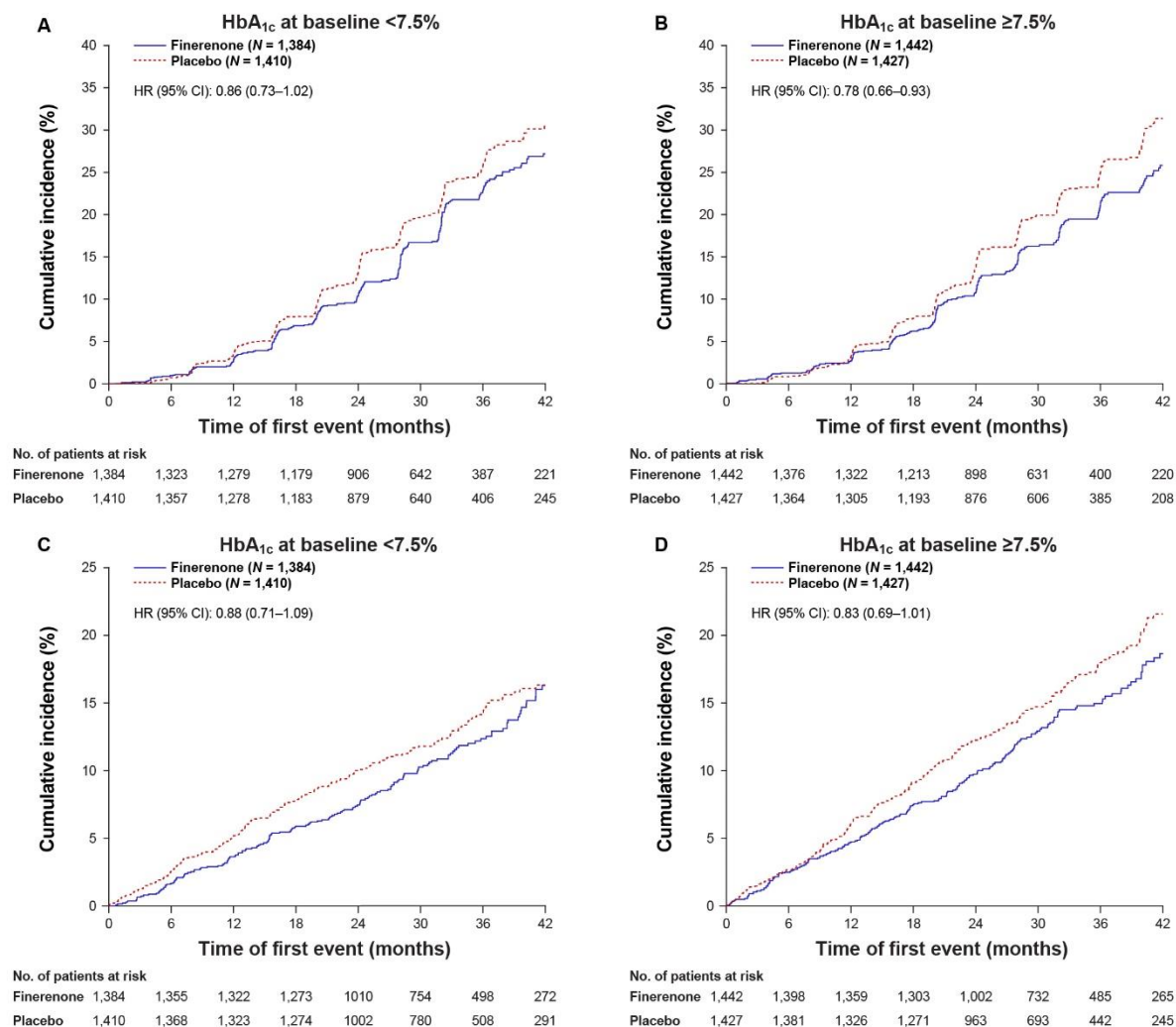


Supplementary Figure 1— Distribution of HbA_{1c} at baseline in both treatment groups.



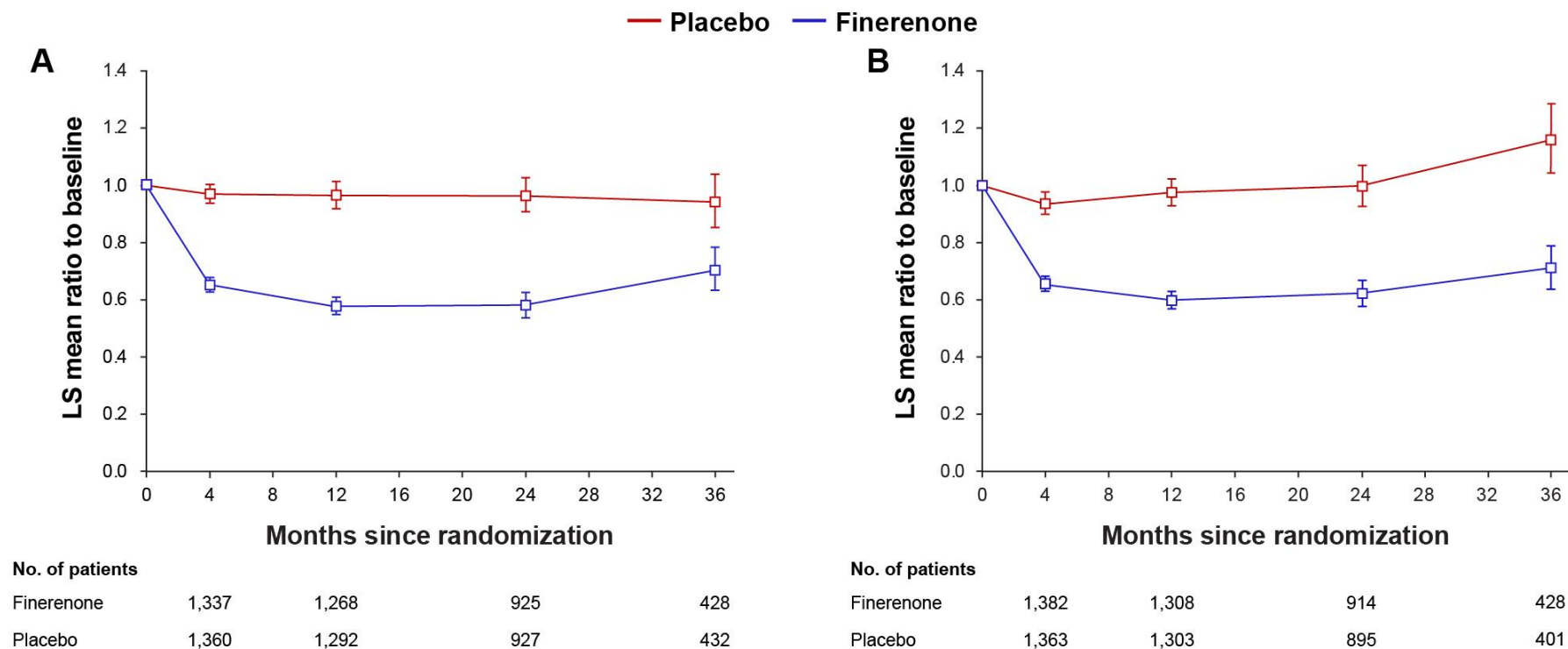
Supplementary Figure 2—Mixed-model analyses of HbA_{1c} over time in patients with a baseline HbA_{1c} <7.5% (**A**) and ≥7.5% (**B**). Analyses included the following covariates: treatment group, stratification factors (region, albuminuria category at screening, and eGFR category at screening), time, treatment over time, baseline value nested within baseline HbA_{1c} category, and baseline value over time.

eGFR, estimated glomerular filtration rate; LS, least-squares; SD, standard deviation.



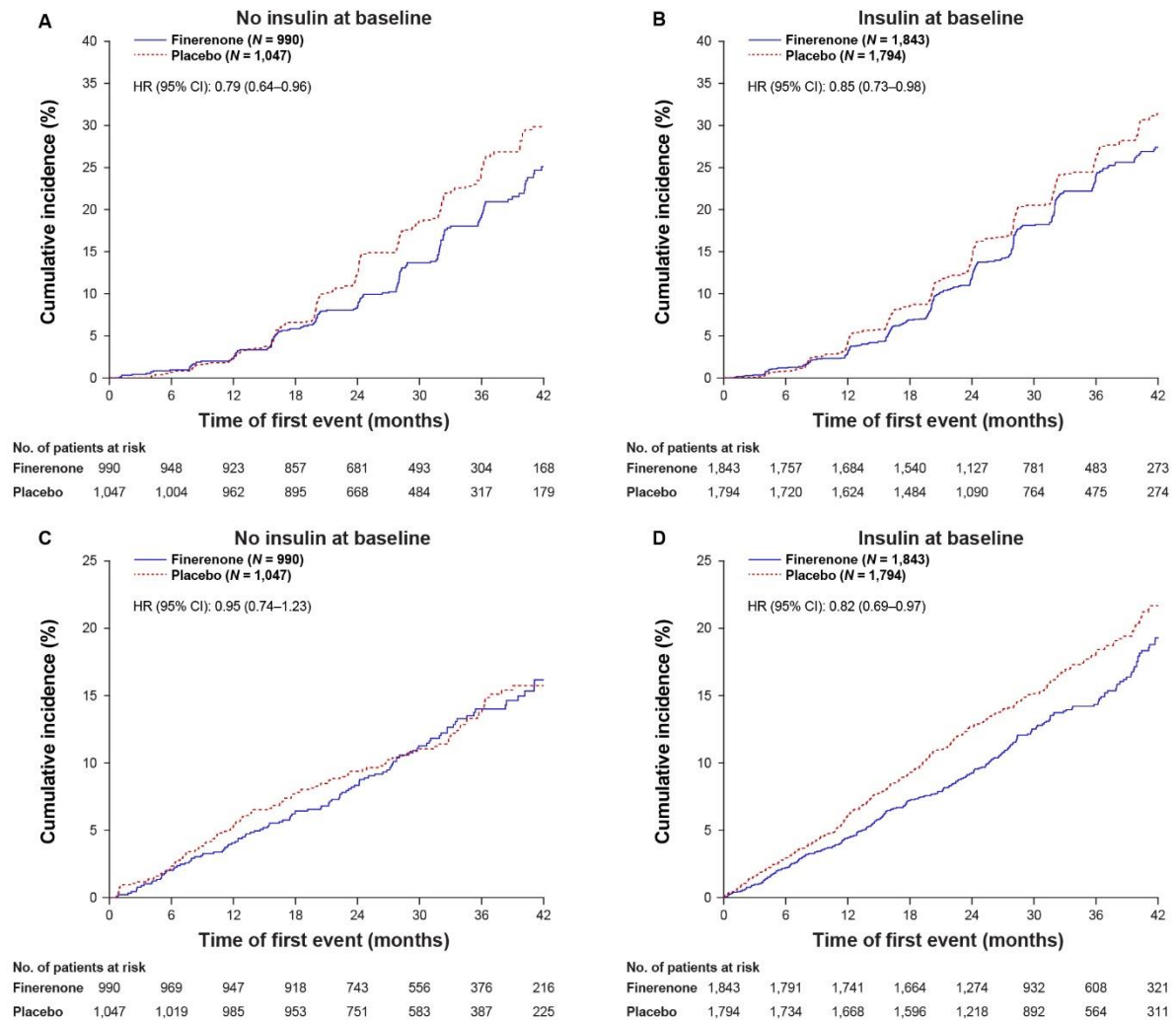
Supplementary Figure 3—Composite kidney and CV outcomes according to HbA_{1c} level at baseline. Panels A and B show the primary kidney composite outcome (time-to first onset of kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death) in patients with a baseline HbA_{1c} <7.5% (**A**) and ≥7.5% (**B**). Panels C and D show the key secondary CV composite outcome (time to first onset of CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure) in patients with a baseline HbA_{1c} <7.5% (**C**) and ≥7.5% (**D**).

CV, cardiovascular; eGFR, estimated glomerular filtration rate.



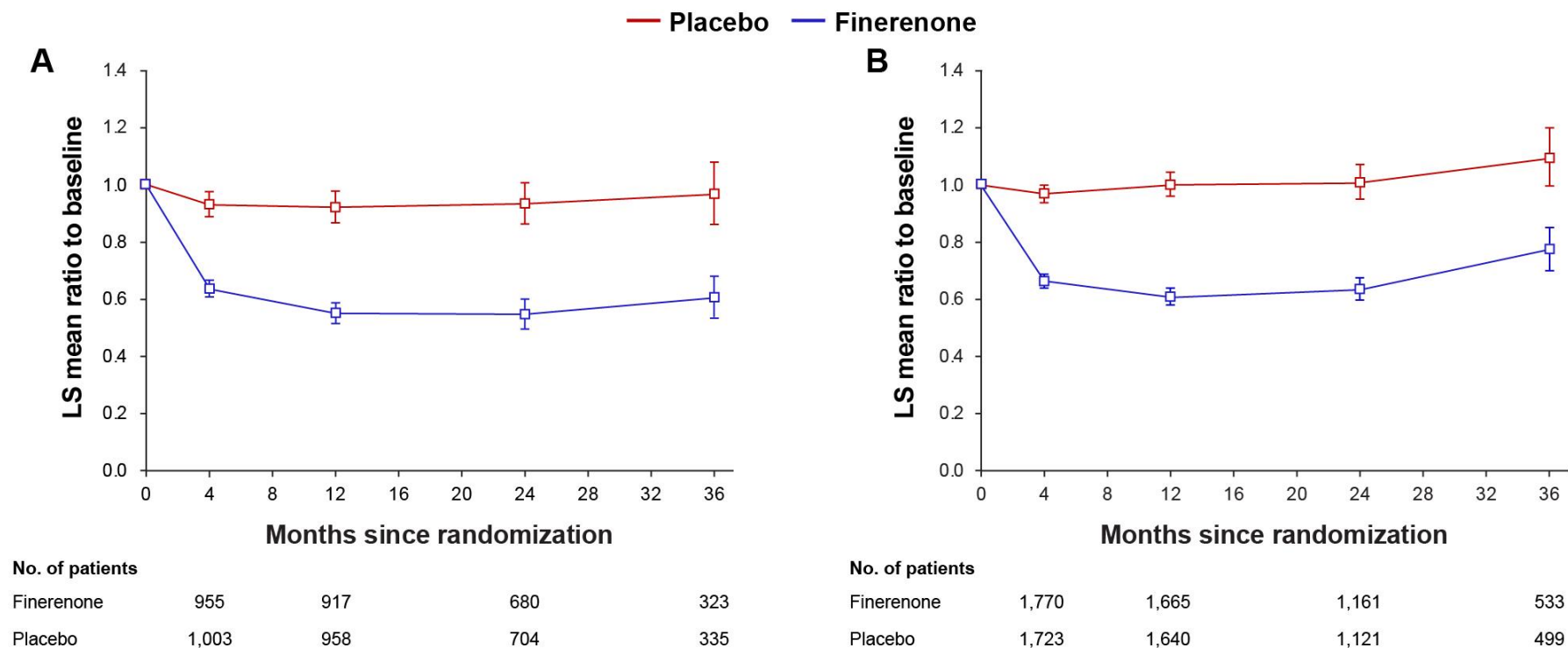
Supplementary Figure 4—Mixed-model analyses of UACR over time in patients with HbA_{1c} <7.5% (**A**) or ≥7.5% (**B**) at baseline (median HbA_{1c} at baseline). Analyses included the following covariates: treatment group, stratification factors (region, albuminuria category at screening, and eGFR category at screening), time, treatment over time, log-transformed baseline value nested within type of albuminuria at screening, and log-transformed baseline value over time.

eGFR, estimated glomerular filtration rate; LS, least squares; UACR, urine albumin-to-creatinine ratio.



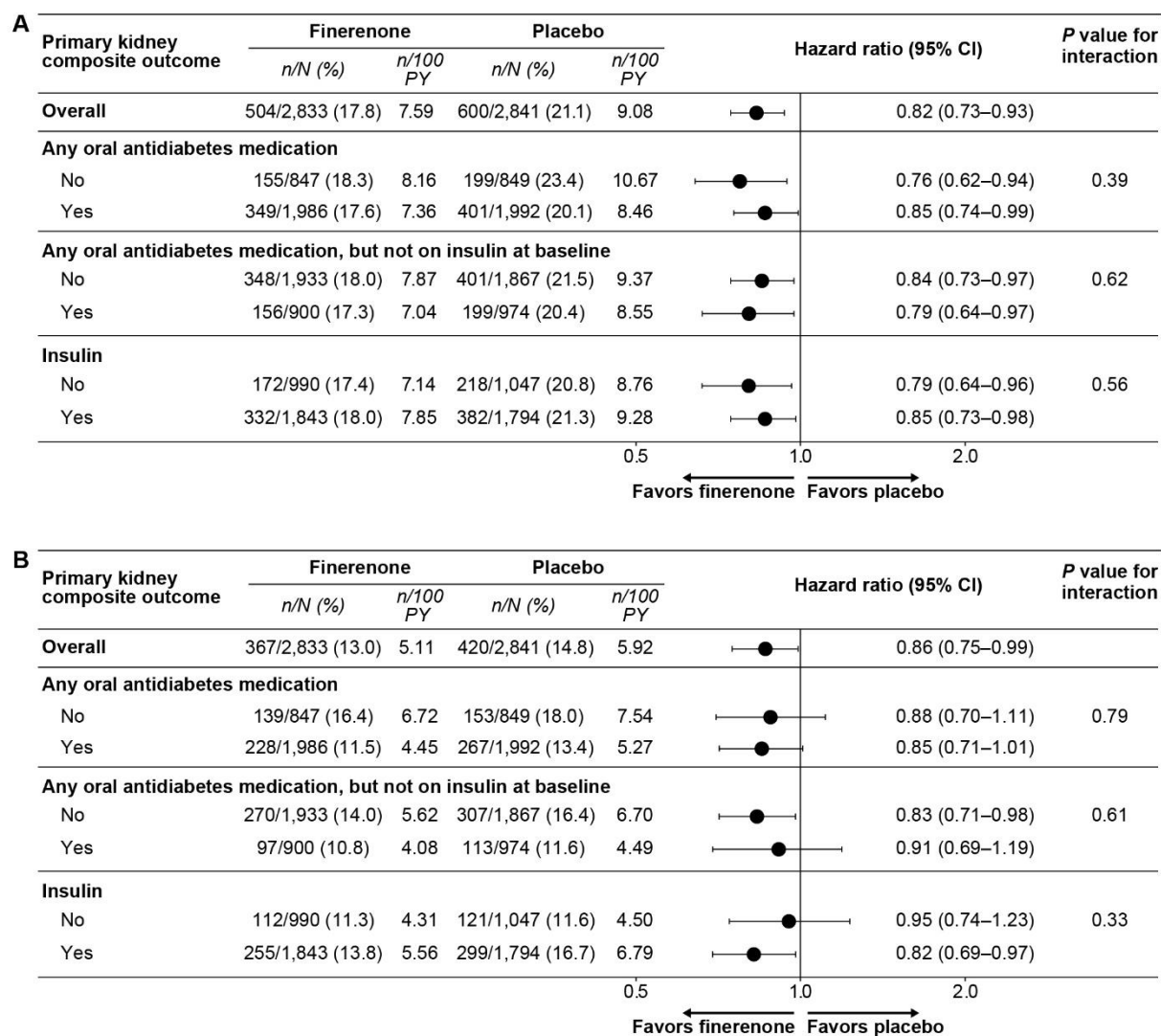
Supplementary Figure 5—Composite kidney and CV outcomes according to insulin use at baseline. Panels A and B show the primary kidney composite outcome (time to first onset of kidney failure, sustained $\geq 40\%$ decrease in eGFR from baseline, or renal death) in patients not treated with insulin at baseline (**A**) and treated with insulin at baseline (**B**). Panels C and D show the key secondary CV composite outcome (time to first onset of CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure) in patients not treated with insulin at baseline (**C**) and treated with insulin at baseline (**D**).

CV, cardiovascular; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

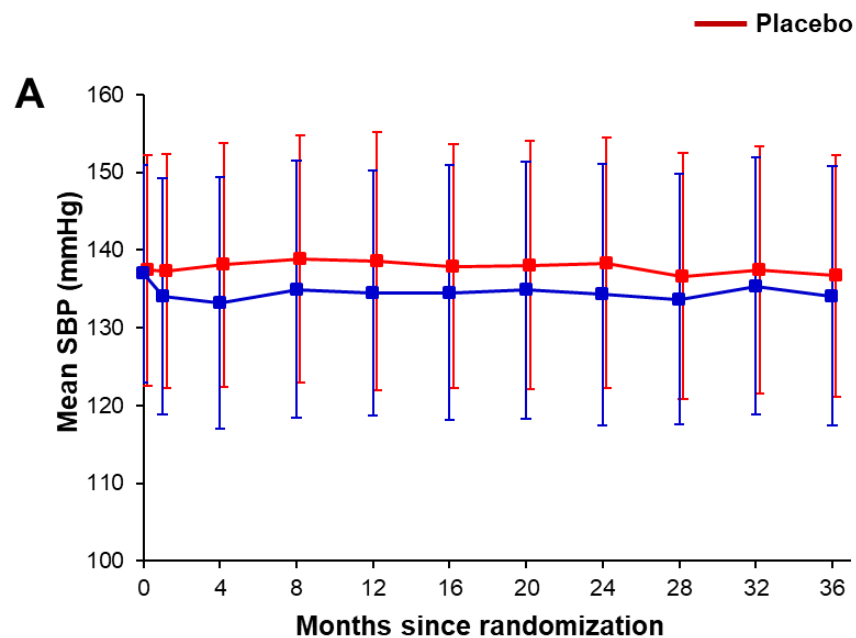


Supplementary Figure 6—Mixed-model analyses of UACR levels in patients without insulin use at baseline (**A**) or patients with insulin use at baseline (**B**). Analyses included the following covariates: treatment group, stratification factors (region, albuminuria category at screening, and eGFR category at screening), time, treatment over time, log-transformed baseline value nested within type of albuminuria at screening, and log-transformed baseline value over time.

eGFR, estimated glomerular filtration rate; LS, least-squares; UACR, urine albumin-to-creatinine ratio.

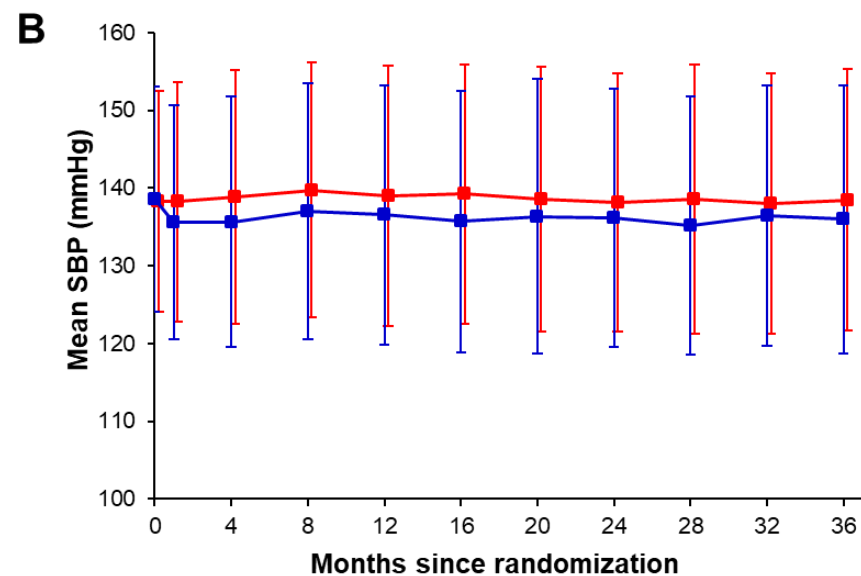


Supplementary Figure 7—Primary kidney composite outcome (time to first onset of kidney failure, sustained $\geq 40\%$ decrease in eGFR from baseline, or renal death) (**A**) and key secondary CV composite outcome (time to first onset of CV death, nonfatal MI, nonfatal stroke, or hospitalization for heart failure) (**B**) according to oral antidiabetic treatment and insulin treatment at baseline. Oral antidiabetic treatments included DDP-4 inhibitors, SGLT-2 inhibitors, biguanides, sulfonylureas, alpha-glucosidase inhibitors, meglitinides, and thiazolidinediones. CV, cardiovascular; DDP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PY, patient-years; SGLT-2, sodium–glucose cotransporter-2.



No. of patients

Finerenone	961	928	707	343
Placebo	1,009	971	725	352

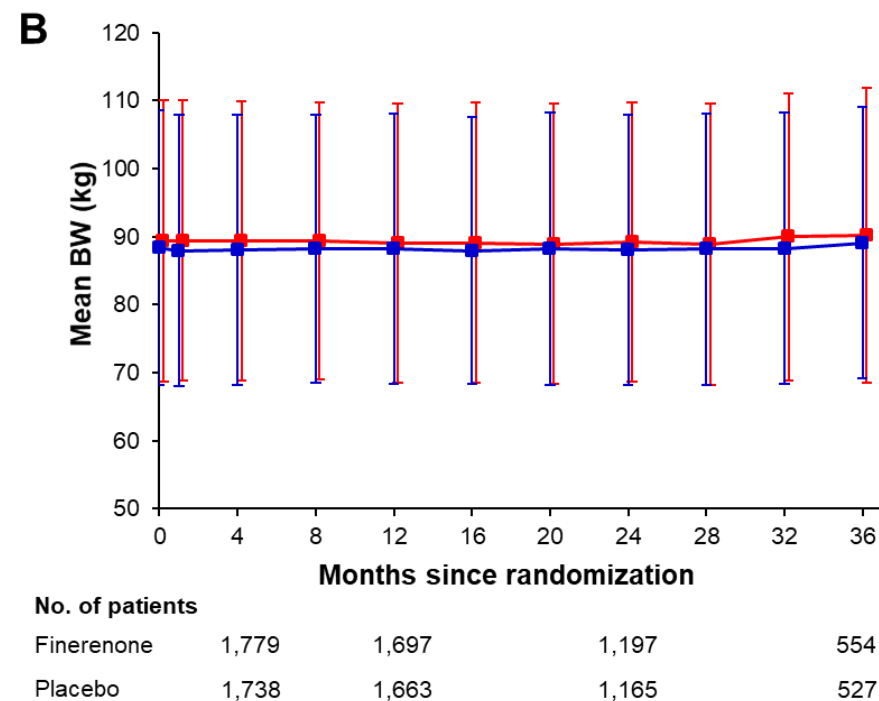
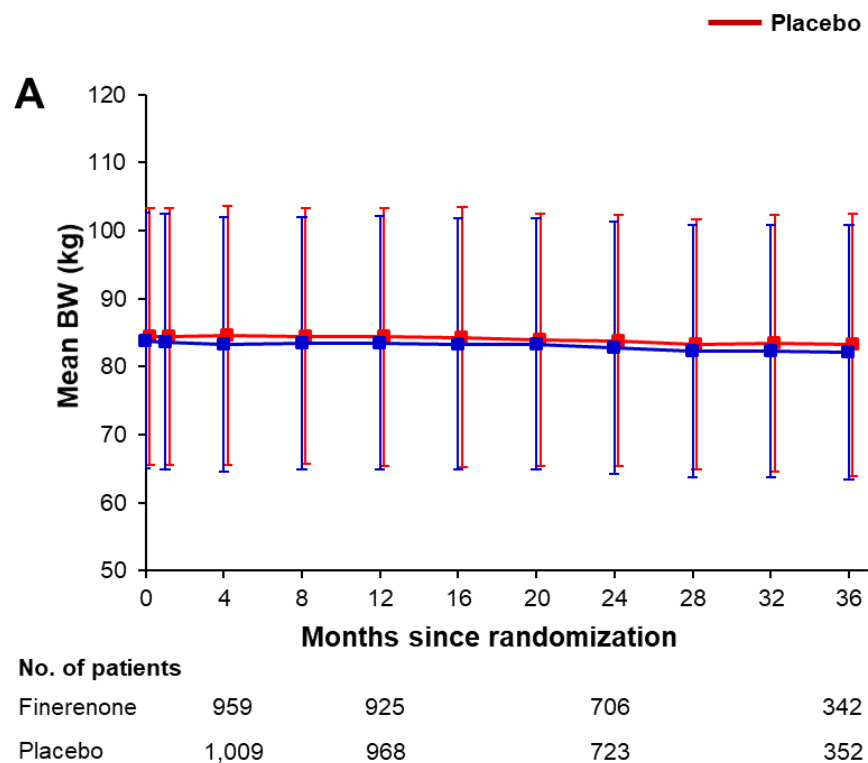


No. of patients

Finerenone	1,785	1,700	1,199	559
Placebo	1,742	1,665	1,170	532

Supplementary Figure 8—Change in systolic blood pressure over time by insulin use at baseline in patients without insulin use at baseline (**A**) or patients with use insulin at baseline (**B**).

SBP; systolic blood pressure



Supplementary Figure 9—Change in body weight over time by insulin use at baseline in patients without insulin use at baseline (**A**) or patients with insulin use at baseline (**B**).

BW, body weight