

SUPPLEMENTARY DATA

Supplementary Table ST1. Participant baseline characteristics by eGFR stage

	Stage eGFR ≥90 ml/min/1.73m ² N=3,325 (22.9%)	1 Stage eGFR 60-89 ml/min/1.73m ² N=7,879 (54.2%)	2 Stage eGFR 45-59 ml/min/1.73m ² N=2,538 (17.5%)	3a Stage eGFR 30-44 ml/min/1.73m ² N=783 (5.4%)	3b
Age (years)	62.4±7.4	65.4±7.7	68.3±7.8	70.1±7.9	
Women	22.8%	28.4%	36.4%	42.0%	
White race	67.9%	67.3%	68.7%	69.3%	
Diabetes duration (years)	10.2±7.2	11.3±7.9	13.1±8.9	15.5±9.2	
<i>Cigarette smoking</i>					
Current	16.6%	11.1%	7.4%	5.9%	
Former	39.2%	40.3%	37.9%	45.1%	
Never	44.2%	48.6%	54.7%	49.0%	
BMI (kg/m ²)	30.0±5.7	30.1±5.4	30.5±5.8	31.1±6.4	
Systolic blood pressure (mmHg)	135±16	135±17	136±18	136±20	
Diastolic blood pressure (mmHg)	78.0±10.0	77.4±10.4	76.7±10.7	73.6±10.9	
HbA _{1c} (%)	7.3±0.5	7.2±0.5	7.2±0.5	7.3±0.5	
HbA _{1c} (mmol/mol)	55.7±5.2	55.5±5.2	55.5±5.2	55.8±5.4	
Total cholesterol (mg/dL)	165±47	166±45	168±46	163±43	
LDL-cholesterol (mg/dL)	90±37	91±37	92±38	87±35	
eGFR (ml/min/1.73m ²)	104±14	73±9	53±4	39±4	
UACR (mg/g)	10.4 (4.4, 30.1)	9.7 (3.5, 30.1)	14.0 (3.6, 54.7)	27.6 (7.8, 132.0)	
<i>Previous vascular disease</i>					
Myocardial infarction	43.9%	41.6%	43.7%	44.2%	
Coronary artery disease	51.0%	52.6%	51.9%	59.3%	
Cerebrovascular disease	22.1%	24.0%	27.7%	28.5%	
Peripheral arterial disease	15.8%	16.3%	17.4%	19.0%	
Heart failure	14.6%	16.8%	22.9%	28.6%	
<i>Glucose-lowering therapies</i>					
Metformin	87.3%	84.5%	74.2%	53.4%	
Sulfonylurea	46.6%	45.0%	45.7%	43.0%	
Thiazolidinedione	2.6%	2.5%	3.2%	3.7%	
Insulin	18.7%	21.6%	27.9%	42.1%	
<i>Cardiovascular medications</i>					
Statin	79.7%	79.8%	80.0%	81.6%	
Aspirin	81.7%	78.2%	76.7%	74.7%	
Thienopyridine	20.5%	22.2%	22.1%	22.1%	
ACEi/ARB	77.5%	78.4%	80.2%	81.7%	
Beta blocker	61.9%	63.3%	65.3%	67.3%	
Calcium channel blocker	31.6%	33.0%	37.4%	41.4%	
Diuretic	32.9%	38.5%	52.6%	63.7%	

Continuous variables are presented as mean ±1SD and categorical variables as percentages. UACR is presented as median (25th, 75th percentiles).

Abbreviations: eGFR = estimated glomerular filtration rate; HbA_{1c} = glycated hemoglobin; UACR = urinary albumin-to-creatinine ratio; BMI = body mass index; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker. Site-reported eGFR values calculated using the Modification of Diet in Renal Disease formula [11]

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Supplementary Table ST2. Association of eGFR stages with cardiovascular endpoints and interaction P values

CV Endpoints n (%)	Stage 1 eGFR ≥ 90 ml/min/1.73m 2			Stage 2 eGFR 60-89 ml/min/1.73m 2			Stage 3a eGFR 45-59 ml/min/1.73m 2			Stage 3b eGFR 30-44 ml/min/1.73m 2			Treatment by eGFR stage Interaction <i>P</i> value
	Sitagliptin	Placebo	Adjusted HR (95% CI)	Sitagliptin	Placebo	Adjusted HR (95% CI)	Sitagliptin	Placebo	Adjusted HR (95% CI)	Sitagliptin	Placebo	Adjusted HR (95% CI)	
4-point MACE	153 (3.30)	177 (3.73)	0.88 (0.71, 1.09)	414 (3.63)	385 (3.46)	1.05 (0.92, 1.21)	184 (5.44)	209 (6.04)	0.94 (0.77, 1.14)	75 (7.22)	70 (7.48)	0.97 (0.70, 1.35)	0.48
3-point MACE	133 (2.85)	148 (3.08)	0.92 (0.73, 1.16)	363 (3.16)	329 (2.93)	1.08 (0.93, 1.25)	167 (4.88)	191 (5.46)	0.93 (0.75, 1.14)	72 (6.89)	69 (7.35)	0.95 (0.68, 1.32)	0.46
CV death	68 (1.39)	68 (1.35)	0.98 (0.70, 1.37)	180 (1.49)	153 (1.28)	1.15 (0.93, 1.43)	88 (2.38)	100 (2.65)	0.97 (0.73, 1.30)	37 (3.25)	42 (4.1)	0.85 (0.54, 1.32)	0.43
Hospitalization for unstable angina	23 (0.48)	34 (0.70)	0.70 (0.41, 1.20)	65 (0.55)	70 (0.61)	0.92 (0.66, 1.30)	20 (0.57)	22 (0.61)	0.93 (0.51, 1.71)	5 (0.45)	2 (0.2)	2.25 (0.44, 11.61)	0.58
Myocardial infarction	57 (1.21)	73 (1.51)	0.82 (0.58, 1.16)	139 (1.19)	142 (1.25)	0.97 (0.77, 1.22)	69 (1.98)	72 (2.01)	1.02 (0.73, 1.42)	32 (3)	25 (2.61)	1.10 (0.65, 1.87)	0.77
Stroke	23 (0.48)	30 (0.61)	0.80 (0.47, 1.38)	97 (0.83)	88 (0.77)	1.07 (0.80, 1.42)	42 (1.19)	50 (1.39)	0.87 (0.58, 1.31)	15 (1.37)	12 (1.23)	1.13 (0.53, 2.41)	0.69
All-cause death	95 (1.94)	91 (1.80)	1.02 (0.77, 1.37)	256 (2.11)	233 (1.96)	1.08 (0.90, 1.29)	125 (3.38)	142 (3.76)	0.96 (0.76, 1.23)	62 (5.44)	68 (6.63)	0.85 (0.60, 1.20)	0.51
Hospitalization for heart failure	25 (0.53)	37 (0.76)	0.68 (0.41, 1.13)	109 (0.93)	105 (0.92)	1.03 (0.79, 1.35)	56 (1.59)	51 (1.42)	1.15 (0.79, 1.69)	35 (3.28)	33 (3.46)	0.94 (0.58, 1.52)	0.52

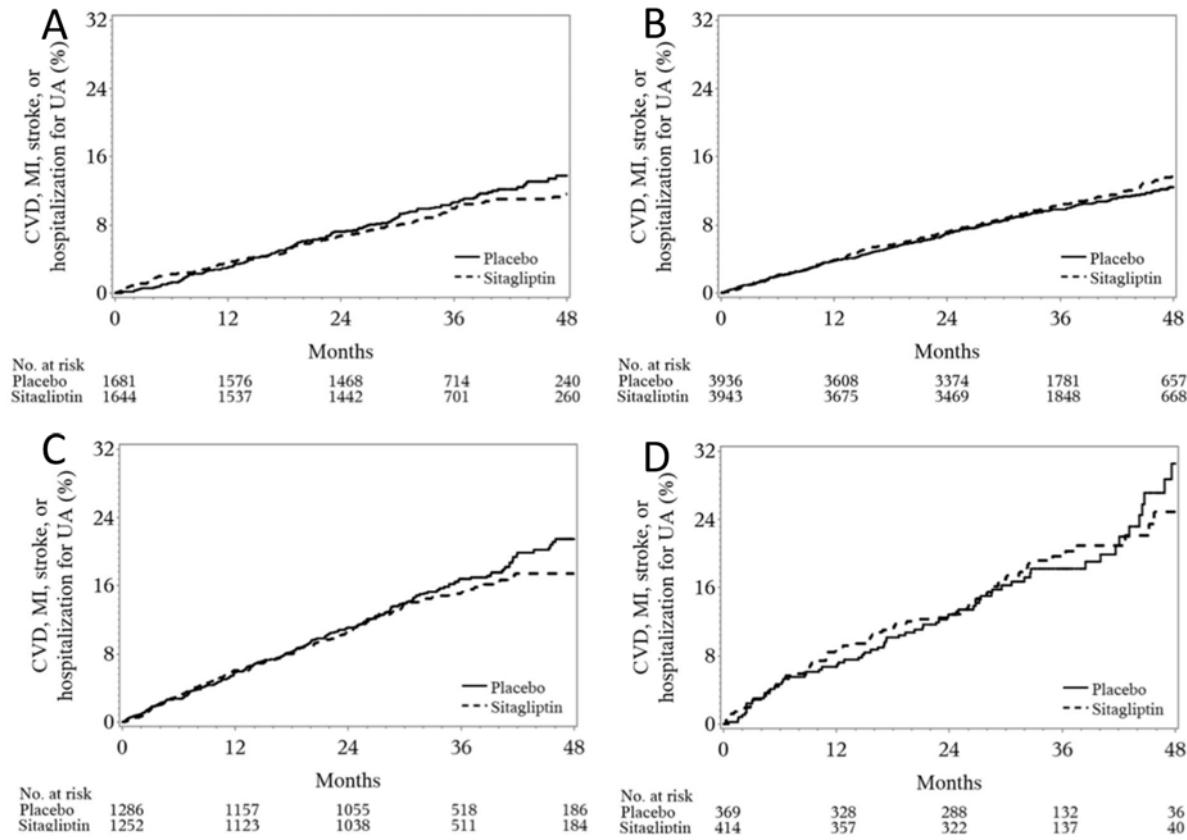
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Supplementary Table ST3. Covariate adjusted between treatment group analysis of mean eGFR changes over 4 years (N=12,937)

	Estimated overall mean difference (95% CI)	P value
Treatment (sitagliptin vs. placebo)	-1.43 (-1.88, -0.98)	<0.0001
Time from randomization when eGFR value measured	-0.07 (-0.08, -0.06)	<0.0001
Baseline eGFR	-0.28 (-0.29, -0.27)	<0.0001
Baseline HbA _{1c}	-0.008 (-0.37, 0.35)	0.97
HbA _{1c} changing over time	-0.19 (-0.31, -0.06)	0.0035
Region (North America as reference)		<0.0001
Asia Pacific and Other	1.68 (0.99, 2.36)	
Eastern Europe	2.96 (2.26, 3.66)	
Latin America	1.13 (0.21, 2.05)	
Western Europe	1.51 (0.70, 2.33)	

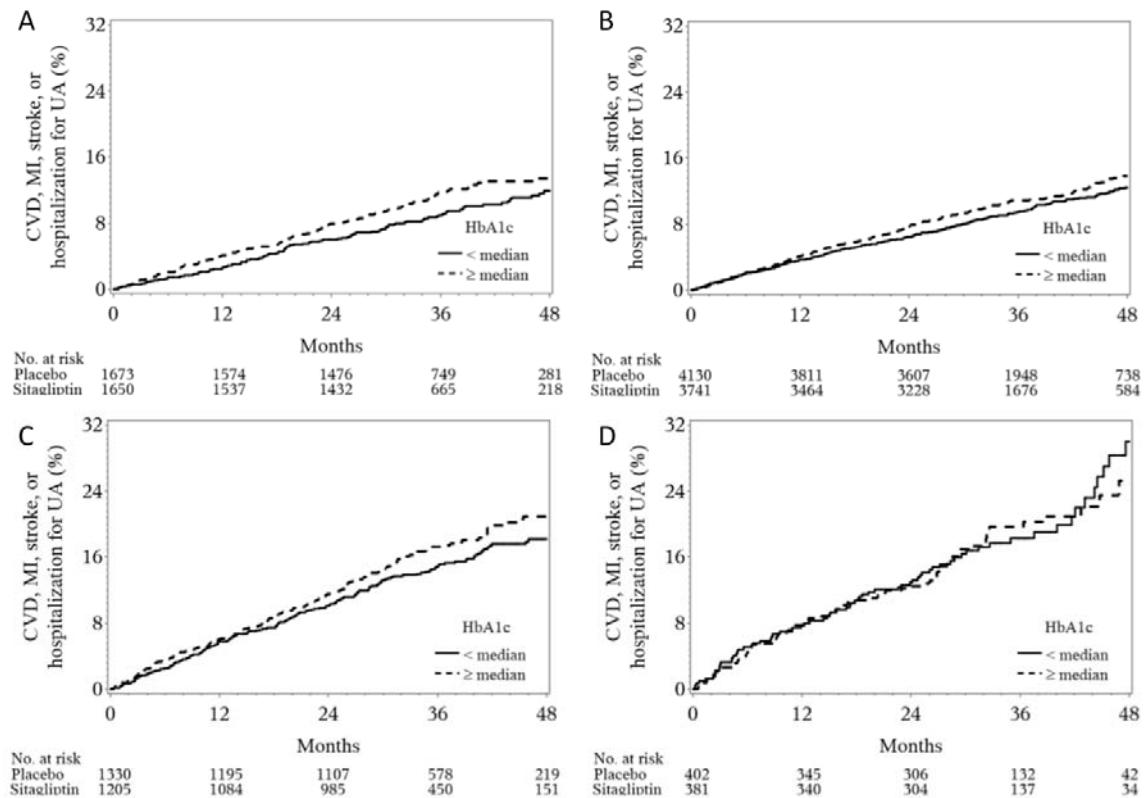
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Supplementary Figure SF1. Kaplan-Meier plots of the primary 4-point primary MACE outcome, split by assigned study treatment, for each baseline eGFR stage: (A) Stage 1, (B) Stage 2, (C) Stage 3a, (D) Stage 3b.



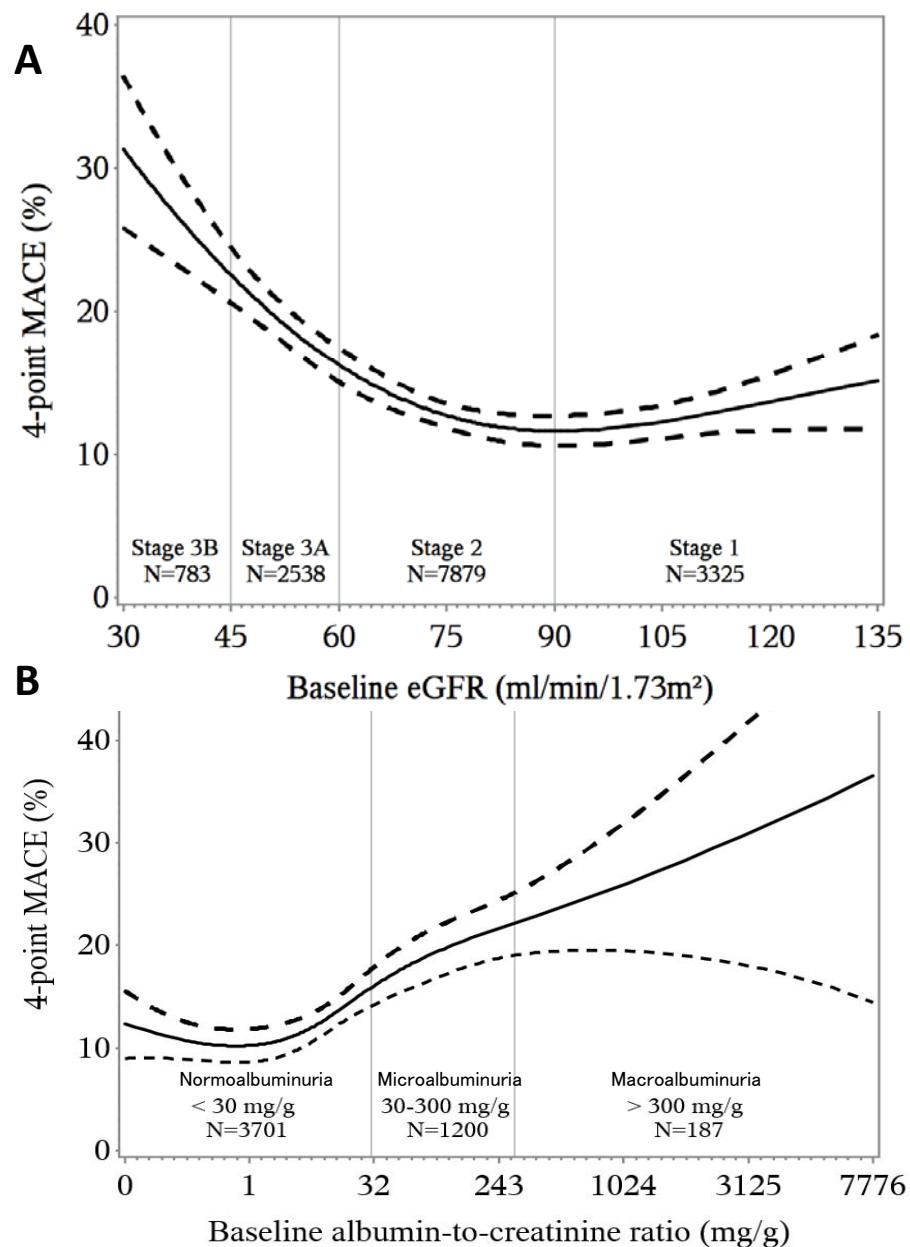
SUPPLEMENTARY DATA

Supplementary Figure SF2. Kaplan-Meier plots of the primary 4-point primary MACE outcome, split by baseline HbA_{1c} values above and below the median, for each baseline eGFR stage: (A) Stage 1, (B) Stage 2, (C) Stage 3a, (D) Stage 3b.



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Supplementary Figure SF3. Associations between primary 4-point MACE cardiovascular outcome and A) baseline eGFR, B) baseline UACR.



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Supplementary Figure SF4. Estimated glomerular filtration rate over 4 years, split by assigned study treatment, for each baseline eGFR stage: (A) Stage 1, (B) Stage 2, (C) Stage 3a, (D) Stage 3b. Data are mean \pm 1 SD.

