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Supplementary Table 1. Relative and absolute effects of canagliflozin on additional kidney, cardiovascular and mortality outcomes in the overall CREDENCE cohort. These results have been previously published.[1]

	Participants with an event per 1000 patient-years		**Hazards Ratio (95% CI)**	**Absolute risk reduction 1000 patients/ 2.6 years (95% CI)**
	Canagliflozin	**Placebo**		
Kidney outcomes				
Kidney failure, doubling of serum creatinine, kidney death, or cardiovascular death	43.2	61.2	0.70 (0.59, 0.82)	-43 (-63, -23)
Kidney failure, doubling of serum creatinine, or kidney death	27.0	40.4	0.66 (0.53, 0.81)	-32 (-49, -16)
Kidney failure or kidney death	20.7	29.6	0.69 (0.54, 0.87)	-22 (-36, -7)
Initiation of kidney replacement therapy, or kidney death	13.6	18.6	0.72 (0.54, 0.97)	-12 (-24, -1)
Kidney failure	20.4	29.4	0.68 (0.54, 0.86)	-22 (-37, -8)
Kidney-related adverse events (including acute kidney injury)	57.1	79.1	0.71 (0.61, 0.82)	-45 (-66, -23)
Cardiovascular outcomes				
Cardiovascular death or hospitalization for heart failure	31.5	45.4	0.69 (0.57, 0.83)	-34 (-51, -16)
Cardiovascular death, myocardial infarction, or stroke	38.7	48.7	0.80 (0.67, 0.95)	-24 (-42, -5)
Hospitalization for heart failure	15.7	25.3	0.61 (0.47, 0.80)	-24 (-37, -11)
Cardiovascular death	19.0	24.4	0.78 (0.61, 1.00)	-14 (-27, 0)
All-cause mortality	29.0	35.0	0.83 (0.43, 1.09)	-15 (-31, 1)

Supplementary Table 2. Relative and absolute effects of canagliflozin on additional kidney, cardiovascular and mortality outcomes by baseline UACR.

	Participants with an event per 1000 patient-years		HR (95% CI)	P value	P-heterogeneity	Absolute risk reduction 1000 patients/ 2.6 years (95% CI)	P-heterogeneity
	Canagliflozin	Placebo					
Doubling of serum creatinine							
All	20.7	33.8	0.60 (0.48, 0.76)	<0.0001		-32 (-47, -17)	
UACR ≤1000 mg/g	5.4	7.5	0.71 (0.38, 1.32)	0.28		-5 (-16, 5)	
UACR >1000 to <3000 mg/g	26.5	41.4	0.62 (0.44, 0.88)	0.008	0.68	-37 (-65, -9)	<0.001
UACR ≥3000 mg/g	88.4	146.2	0.56 (0.39, 0.80)	0.001		-107 (-183, -32)	
Kidney failure, kidney death or cardiovascular death							
All	37.6	51.2	0.73 (0.61, 0.87)	<0.001		-33 (-52, -15)	
UACR ≤1000 mg/g	19.4	25.8	0.75 (0.54, 1.05)	0.10		-16 (-36, 3)	
UACR >1000 to <3000 mg/g	45.9	57.0	0.79 (0.60, 1.04)	0.10	0.59	-28 (-61, 6)	0.11
UACR ≥3000 mg/g	112.0	162.0	0.65 (0.47, 0.89)	0.008		-96 (-176, -16)	
Cardiovascular death, myocardial infarction, stroke, hospitalization for heart failure or hospitalized unstable angina							
All	49.4	66.9	0.74 (0.63, 0.86)	<0.001		-40 (-61, -19)	
UACR ≤1000 mg/g	39.8	54.5	0.73 (0.58, 0.93)	0.01		-35 (-62, -9)	
UACR >1000 to <3000 mg/g	53.9	73.2	0.74 (0.57, 0.95)	0.02	0.95	-43 (-79, -7)	0.95
UACR ≥3000 mg/g	86.5	108.3	0.80 (0.55, 1.17)	0.25		-42 (-114, 31)	

Supplementary Table 3. Effects of canagliflozin on eGFR slope (total, acute and chronic) by baseline UACR. The acute, chronic and total mean change in estimated Glomerular Filtration Rate (eGFR) and standard error (SE) in each treatment group (canagliflozin or placebo) according to UACR category are presented.

UACR categories	Canagliflozin		Placebo		Placebo-subtracted difference (95% CI)	P value‡	P-heterogeneity
	Mean (SE) eGFR change	P value†	Mean (SE) eGFR change	P value†			
Acute slope: eGFR Change from baseline to Week 3 (mL/min/1.73 m^2)							
≤1000 mg/g	-3.15 (0.35)	0.07	0.45 (0.36)	<0.001	-3.60 (-4.58, -2.62)	<0.001	0.44
>1000-<3000 mg/g	-4.13 (0.36)		-1.29 (0.36)		-2.84 (-3.84, -1.83)	<0.001	
≥3000 mg/g	-4.70 (0.77)		-2.26 (0.72)		-2.44 (-4.52, -0.36)	0.02	
Chronic slope: Annual eGFR change from Week 3 to last available measurement (mL/min/1.73 m^2/year)							
≤1000 mg/g	-0.78 (0.15)	<0.001	-3.09 (0.16)	<0.001	2.31 (1.88, 2.73)	<0.001	0.04
>1000-<3000 mg/g	-2.65 (0.22)		-5.94 (0.23)		3.29 (2.67, 3.91)	<0.001	
≥3000 mg/g	-6.43 (0.55)		-8.92 (0.53)		2.49 (1.00, 3.99)	0.001	
Total slope: Annual eGFR change from baseline to Week 130 (mL/min/1.73 m^2/year)							
≤1000 mg/g	-1.88 (0.17)	<0.001	-2.79 (0.18)	<0.001	0.91 (0.42, 1.40)	0.0003	0.008
>1000-<3000 mg/g	-4.15 (0.24)		-6.37 (0.25)		2.23 (1.55, 2.90)	<0.001	
≥3000 mg/g	-8.15 (0.60)		-9.68 (0.57)		1.53 (-0.11, 3.17)	0.07	

eGFR, estimated Glomerular Filtration Rate; SE, standard error; CI, confidence interval.
The effects of canagliflozin on the mean on-treatment eGFR slope were analysed using a 2-slope linear spline model for mean eGFR, with a knot at Week 3 to account for separate acute (randomization to Week 3) and chronic (Week 3 to end of follow-up) slopes. The full model also included random intercepts, acute and chronic slopes. The mean total slope was computed as a weighted combination of the acute and chronic slopes to reflect the mean rate of eGFR change to Week 130.
†P value for comparison between UACR categories
‡P value for effect of canagliflozin on eGFR slope in each UACR category

Supplementary Table 4. Relative and absolute effects of canagliflozin on kidney safety outcomes by baseline UACR.

	Participants with an event per 1000 patient-years		HR (95% CI)	P value	P-heterogeneity	Absolute risk reduction 1000 patients/ 2.6 years (95% CI)	P-heterogeneity
	Canagliflozin	Placebo					
Acute kidney injury							
All	16.9	20.0	0.85 (0.64, 1.13)	0.27		-6 (-17, 6)	
UACR ≤1000 mg/g	15.8	15.2	1.05 (0.69, 1.61)	0.81		3 (-12, 18)	
UACR >1000 to <3000 mg/g	19.4	22.5	0.85 (0.54, 1.36)	0.51	0.12	-6 (-27, 15)	0.11
UACR ≥3000 mg/g	14.5	36.1	0.40 (0.17, 0.95)	0.04		-40 (-77, -3)	
Volume depletion							
All	28.4	23.5	1.25 (0.97, 1.59)	0.08		13 (-1, 27)	
UACR ≤1000 mg/g	28.2	23.8	1.23 (0.88, 1.70)	0.22		12 (-7, 32)	
UACR >1000 to <3000 mg/g	30.2	23.1	1.34 (0.89, 2.03)	0.16	0.84	17 (-7, 40)	0.82
UACR ≥3000 mg/g	22.8	22.8	1.01 (0.44, 2.29)	0.98		3 (-34, 39)	
Hyperkalemia							
All	29.7	36.9	0.80 (0.65, 1.00)	0.05		-14 (-29, 2)	
UACR ≤1000 mg/g	22.9	32.3	0.70 (0.51, 0.97)	0.03		-20 (-40, 0)	
UACR >1000 to <3000 mg/g	34.8	40.3	0.86 (0.61, 1.21)	0.39	0.46	-11 (-39, 16)	0.53
UACR ≥3000 mg/g	51.8	49.4	1.00 (0.58, 1.74)	1.00		11 (-42, 64)	
Urinary tract infection							
All	48.3	45.1	1.08 (0.90, 1.29)	0.42		11 (-7, 29)	
UACR ≤1000 mg/g	44.0	42.0	1.05 (0.81, 1.35)	0.72		8 (-16, 33)	
UACR >1000 to <3000 mg/g	50.2	45.7	1.11 (0.82, 1.51)	0.50	0.93	12 (-19, 42)	0.90
UACR ≥3000 mg/g	66.3	58.9	1.15 (0.70, 1.88)	0.58		23 (-35, 81)	
Hypoglycemia							
All	44.3	48.9	0.92 (0.77, 1.11)	0.39		-7 (-25, 11)	
UACR ≤1000 mg/g	45.4	45.7	1.03 (0.80, 1.32)	0.83		3 (-22, 28)	
UACR >1000 to <3000 mg/g	41.1	55.8	0.73 (0.54, 0.99)	0.05	0.15	-31 (-62, 0)	0.14
UACR ≥3000 mg/g	49.7	43.7	1.18 (0.67, 2.10)	0.57		18 (-33, 69)	

Supplementary Table 5. Effects of canagliflozin on the intermediate outcomes of glycated haemoglobin (HbA1c), body weight and systolic blood pressure by baseline UACR.

	UACR ≤1000 mg/g		**UACR >1000-<3000 mg/g**		**UACR ≥3000 mg/g**	
	Canagliflozin	**Placebo**	**Canagliflozin**	**Placebo**	**Canagliflozin**	**Placebo**
HbA1c, %, n	1066	1060	846	847	239	241
Mean (SD) baseline	8.2 (1.2)	8.2 (1.3)	8.3 (1.3)	8.3 (1.3)	8.4 (1.5)	8.4 (1.3)
LS mean change (SE)	-0.42 (0.03)	-0.09 (0.03)	-0.43 (0.03)	-0.24 (0.03)	-0.39 (0.08)	-0.27 (0.08)
Difference vs placebo (95% CI)	-0.33 (-0.40, -0.26)		-0.18 (-0.26, -0.10)		-0.12 (-0.30, 0.06)	
Body weight, kg, n	1079	1072	850	852	247	249
Mean (SD) baseline	87.7 (20.3)	86.7 (20.3)	87.8 (21.3)	86.7 (20.6)	83.6 (20.1)	88.3 (22.4)
LS mean change (SE)	-1.34 (0.09)	-0.53 (0.09)	-0.92 (0.12)	-0.09 (0.11)	-0.87 (0.21)	-0.15 (0.21)
Difference vs placebo (95% CI)	-0.81 (-0.97, -0.66)		-0.84 (-1.02, -0.66)		-0.72 (-1.05, -0.38)	
Systolic blood pressure, mmHg, n	1081	1072	850	853	247	249
Mean (SD) baseline	138 (15)	139 (15)	141 (16)	141 (16)	141 (16)	144 (15)
LS mean change (SE)	-3.22 (0.31)	0.44 (0.31)	-2.75 (0.36)	0.67 (0.36)	-1.44 (0.74)	-0.55 (0.75)
Difference vs placebo (95% CI)	-3.66 (-4.45, -2.86)		-3.41 (-4.34, -2.49)		-0.90 (-2.67, 0.88)	

Reference

1. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. *N Engl J Med.* 2019;380(24):2295-2306.