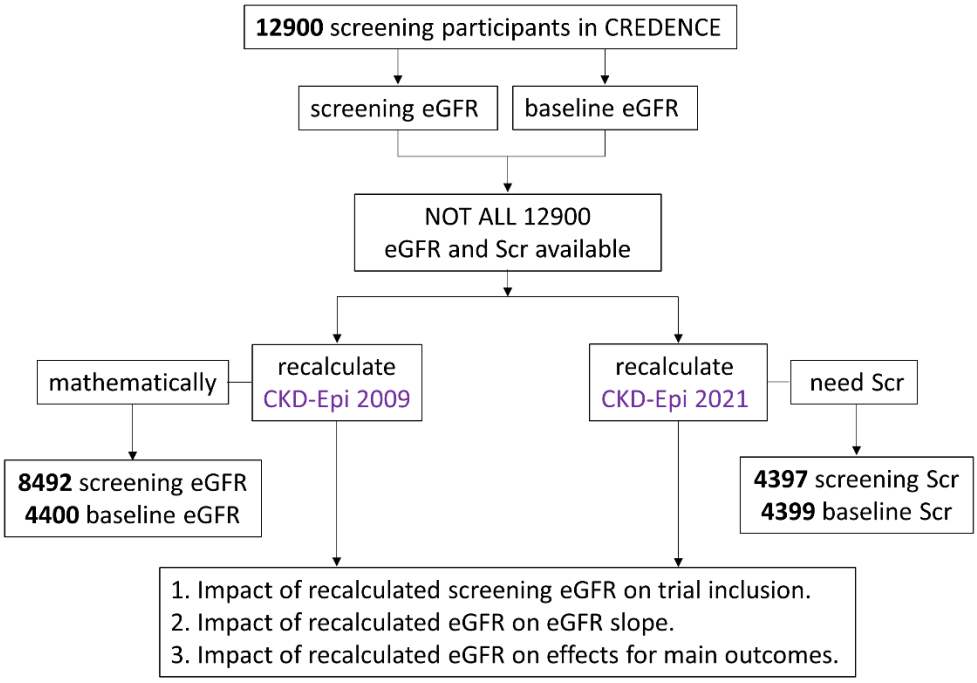
Supplemental Material

Supplemental Figure 1. Data sources and recalculation of eGFR according to the 2009 and 2021 CKD Epi creatinine equations.



Supplemental Table 1. Baseline characteristics of Black and non-Black participants in the CREDENCE Trial according randomized therapy.

	Black		Non-Black[1]	
	canagliflozin (n=112)	Placebo (n=112)	canagliflozin (n=2090)	Placebo (n=2087)
Age, years, mean (SD)	62 (10)	60 (10)	62 (9)	63 (9)
Male, no. (%)	63 (56)	59 (53)	1377 (66)	1408 (67)
Current smoker, no. (%)	14 (13)	15 (13)	327 (16)	283 (14)
Duration of diabetes, years, mean (SD)	17.5 (8.9)	16.4 (9.8)	15.4 (8.7)	16.0 (8.5)
Hypertension, no. (%)	112 (100)	110 (98)	2019 (97)	2019 (97)
MI, no. (%)	7 (6)	11 (10)	208 (10)	216 (10)
Heart failure, no. (%)	14 (13)	13 (12)	315 (15)	310 (15)
Microvascular disease, %				
Retinopathy	33 (29)	34 (30)	902 (43)	913 (44)
Nephropathy	112 (100)	112 (100)	2090 (100)	2087 (100)
Neuropathy	61 (54)	59 (53)	1016 (49)	1011 (48)
Atherosclerotic vascular disease, no. (%)[2]				
Coronary	28 (25)	31 (28)	625 (30)	629 (30)
Cerebrovascular	18 (16)	11 (10)	324 (16)	347 (17)
Peripheral	26 (23)	24 (21)	505 (24)	491 (24)
Fracture, no. (%)	23 (21)	14 (13)	313 (15)	360 (17)
Amputation, no. (%)	5 (4)	8 (7)	114 (5)	107 (5)
BMI, kg/m^2, mean (SD)	34 (7)	35 (8)	31 (6)	31 (6)
systolic blood pressure, mmHg, mean (SD)	142 (18)	143 (17)	140 (15)	140 (16)
diastolic blood pressure, mmHg, mean (SD)	78 (10)	80 (10)	78 (9)	78 (9)
HbA1c, %, mean (SD)	8.4 (1.3)	8.4 (1.3)	8.3 (1.3)	8.3 (1.3)
Cholesterol, mg/dL, mean (SD)				
Total	181 (50)	178 (42)	181 (50)	178 (50)
LDL	100 (42)	100 (39)	97 (42)	97 (39)
HDL	46 (15)	46 (15)	42 (15)	42 (12)
TG, mg/dL, mean (SD)	177 (142)	159 (97)	204 (142)	195 (150)
Baseline eGFR, mL/min/1.73 m^2, mean (SD)				
2009 CKD-Epi creatinine	53 (17)	57 (18)	56 (18)	56 (18)
2009 CKD-Epi creatinine without a race specific coefficient	46 (14)	49 (16)	56 (18)	56 (18)
2021 CKD-Epi creatinine	49 (14)	52 (14)	59 (18)	59 (18)
UACR, mg/g, median (IQR)	706 (398-1587)	702 (418-1445)	928 (463-1807)	943 (483-1912)
Albuminuria, no (%)				
Normal	0 (0)	0 (0)	16 (0.8)	15 (0.7)
Microalbuminuria	21 (19)	15 (13)	230 (11)	230 (11)
Macroalbuminuria	91 (81)	97 (87)	1844 (88)	1842 (88)
Drug therapy, no. (%)				
Insulin	90 (80)	82 (73)	1362 (65)	1350 (65)
Sulfonylurea	29 (26)	33 (29)	583 (28)	623 (30)
Metformin	51 (46)	56 (50)	1225 (59)	1213 (58)
GLP-1 receptor agonist	7 (6)	8 (7)	82 (4)	86 (4)
Statin	80 (71)	69 (62)	1458 (70)	1429 (68)
Antithrombotic[3]	64 (57)	62 (55)	1277 (61)	1221 (59)
RAAS inhibitor	111 (99)	111 (99)	2090 (100)	2083 (99.8)
β-Blocker	52 (46)	48 (43)	831 (40)	839 (40)
Diuretic	66 (59)	72 (64)	960 (46)	959 (46)

SD, standard deviation; MI, myocardial infarction; BMI, body mass index; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; IQR, interquartile range; GLP-1, glucagon-like peptide-1; RAAS, renin-angiotensin-aldosterone system.

[1]Includes White, Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, multiple, other, and unknown.

[2]Some patients had more than one type of atherosclerotic disease.

[3]Includes antiplatelets and anticoagulants.

Supplemental Table 2. Baseline characteristics of screened participants overall and for Black individuals meeting eGFR exclusion criteria with original or recalculated eGFR (2009 CKD-Epi) ≥ 90 mL/min/1.73 m^2.

	overall		Black	
	Original (n=835)	Recalculated (n=808)	Original (n=46)	Recalculated (n=19)
Age, years, mean (SD)	56 (9)	56 (9)	59 (10)	55 (9)
Male, no. (%)	480 (57)	460 (57)	32 (70)	12 (63)
Cardiovascular disease, no. (%)	4 (0.5)	4 (0.5)	0 (0)	0 (0)
Fracture, no. (%)	0 (0)	0 (0)	0 (0)	0 (0)
Screening eGFR original, mL/min/1.73 m^2, mean (SD)	99 (8)	99 (8)	103 (9)	112 (8)
Screening eGFR recalculated, mL/min/1.73 m^2, mean (SD)	99 (8)	99 (8)	89 (8)	97 (7)
Screening UACR, mg/g, median (IQR)	411 (105-1075)	413 (105-1094)	332 (105-741)	324 (103-593)
Albuminuria, no (%)				
Normal	138 (17)	132 (16)	8 (17)	2 (11)
Microalbuminuria	223 (27)	215 (27)	14 (30)	6 (32)
Macroalbuminuria	474 (57)	461 (57)	24 (52)	11 (58)
Drug therapy, no. (%)				
Insulin	3 (0.4)	3 (0.4)	0 (0)	0 (0)
Sulfonylurea	3 (0.4)	3 (0.4)	0 (0)	0 (0)
Metformin	10 (1)	10 (1)	0 (0)	0 (0)
GLP-1 receptor agonist	1 (0.1)	1 (0.1)	0 (0)	0 (0)
Statin	1 (0.1)	1 (0.1)	0 (0)	0 (0)
Antithrombotic[1]	2 (0.2)	2 (0.2)	0 (0)	0 (0)
RAAS inhibitor	6 (0.7)	6 (0.7)	0 (0)	0 (0)
β-Blocker	2 (0.2)	2 (0.2)	0 (0)	0 (0)
Diuretic	1 (0.1)	1 (0.1)	0 (0)	0 (0)

SD, standard deviation; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; IQR, interquartile range; GLP-1, glucagon-like peptide-1; RAAS, renin-angiotensin-aldosterone system.
[1]Includes antiplatelets and anticoagulants.

Supplemental Table 3. Baseline characteristics of screened participants overall and for Black individuals meeting eGFR exclusion criteria with original or recalculated eGFR (2009 CKD-Epi) < 30 mL/min/1.73 m^2.

	overall		Black	
	Original (n=608)	Recalculated (n=644)	Original (n=46)	Recalculated (n=82)
Age, years, mean (SD)	63 (10)	63 (10)	63 (11)	63 (10)
Male, no. (%)	355 (58)	374 (58)	22 (48)	41 (50)
Cardiovascular disease, no. (%)	7 (1)	17 (3)	0 (0)	10 (12)
Fracture, no. (%)	1 (0.2)	5 (0.8)	0 (0)	4 (5)
Screening eGFR original, mL/min/1.73 m^2, mean (SD)	23 (5)	24 (5)	25 (4)	28 (5)
Screening eGFR recalculated, mL/min/1.73 m^2, mean (SD)	23 (5)	23 (5)	21 (3)	24 (4)
Screening UACR, mg/g, median (IQR)	1339 (492-2866)	1315 (496-2861)	936 (462-1486)	944 (470-1685)
Albuminuria, no (%)				
Normal	19 (3)	21 (3)	1 (2)	3 (4)
Microalbuminuria	84 (14)	87 (14)	7 (15)	10 (12)
Macroalbuminuria	505 (83)	536 (83)	38 (83)	69 (84)
Drug therapy, no. (%)				
Insulin	14 (2)	30 (5)	0 (0)	16 (20)
Sulfonylurea	4 (0.7)	11 (2)	0 (0)	7 (9)
Metformin	2 (0.3)	9 (1)	0 (0)	7 (9)
GLP-1 receptor agonist	0 (0)	3 (0.5)	0 (0)	3 (4)
Statin	6 (1)	25 (4)	0 (0)	19 (23)
Antithrombotic[1]	5 (0.8)	19 (3)	0 (0)	14 (17)
RAAS inhibitor	8 (1)	30 (5)	0 (0)	22 (27)
β-Blocker	4 (0.7)	18 (3)	0 (0)	14 (17)
Diuretic	3 (0.5)	20 (3)	0 (0)	17 (21)

SD, standard deviation; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; IQR, interquartile range; GLP-1, glucagon-like peptide-1; RAAS, renin-angiotensin-aldosterone system.
[1]Includes antiplatelets and anticoagulants.

Supplemental Table 4. Baseline characteristics of screened participants meeting eGFR inclusion criteria according to original or recalculated eGFR (2009 CKD-Epi).

	eGFR ≥60 to <90 mL/min/1.73 m^2		eGFR ≥45 to <60 mL/min/1.73 m^2		eGFR ≥30 to <45 mL/min/1.73 m^2	
	Original (n=2876)	Recalculated (n=2822)	Original (n=2007)	Recalculated (n=2015)	Original (n=2166)	Recalculated (n=2203)
Age, years, mean (SD)	62 (9)	62 (9)	63 (9)	63 (9)	64 (10)	64 (10)
Male, no. (%)	1859 (65)	1827 (65)	1313 (65)	1317 (65)	1398 (65)	1427 (65)
Cardiovascular disease, no. (%)	893 (31)	880 (31)	648 (32)	649 (32)	684 (32)	686 (31)
Fracture, no. (%)	299 (10)	297 (11)	203 (10)	202 (10)	209 (10)	208 (9)
Screening eGFR original, mL/min/1.73 m^2, mean (SD)	73 (8)	74 (9)	52 (4)	52 (5)	37 (4)	37 (5)
Screening eGFR recalculated, mL/min/1.73 m^2, mean (SD)	72 (9)	73 (8)	51 (5)	52 (4)	37 (4)	37 (4)
Screening UACR, mg/g, median (IQR)	685 (334-1452)	687 (336-1454)	817 (369-1812)	818 (361-1812)	1032 (427-2261)	1007 (418-2209)
Albuminuria, no (%)						
Normal	156 (5)	156 (6)	85 (4)	88 (4)	74 (3)	75 (3)
Microalbuminuria	499 (17)	484 (17)	297 (15)	299 (15)	283 (13)	301 (14)
Macroalbuminuria	2221 (77)	2182 (77)	1625 (81)	1628 (81)	1809 (84)	1827 (83)
Drug therapy, no. (%)						
Insulin	1081 (38)	1047 (37)	877 (44)	892 (44)	946 (44)	949 (43)
Sulfonylurea	599 (21)	596 (21)	353 (18)	346 (17)	343 (16)	346 (16)
Metformin	1383 (48)	1367 (48)	748 (37)	750 (37)	443 (20)	450 (20)
GLP-1 receptor agonist	87 (3)	84 (3)	44 (2)	46 (2)	53 (2)	51 (2)
Statin	1198 (42)	1175 (42)	902 (45)	903 (45)	939 (43)	942 (43)
Antithrombotic[1]	1058 (37)	1040 (37)	758 (38)	762 (38)	814 (38)	814 (37)
RAAS inhibitor	1829 (64)	1792 (64)	1281 (64)	1288 (64)	1301 (60)	1309 (59)
β-Blocker	636 (22)	622 (22)	518 (26)	521 (26)	620 (29)	617 (28)
Diuretic	736 (26)	711 (25)	606 (30)	617 (31)	720 (33)	717 (33)

SD, standard deviation; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; IQR, interquartile range; GLP-1, glucagon-like peptide-1; RAAS, renin-angiotensin-aldosterone system.

[1]Includes antiplatelets and anticoagulants.

Supplemental Table 5. Baseline characteristics of Black screened participants meeting eGFR inclusion criteria according to original or recalculated eGFR (2009 CKD-Epi).

	eGFR ≥60 to <90 mL/min/1.73 m^2		eGFR ≥45 to <60 mL/min/1.73 m^2		eGFR ≥30 to <45 mL/min/1.73 m^2	
	Original (n=174)	Recalculated (n=120)	Original (n=141)	Recalculated (n=149)	Original (n=117)	Recalculated (n=154)
Age, years, mean (SD)	60 (9)	59 (10)	62 (10)	61 (9)	63 (11)	63 (11)
Male, no. (%)	103 (59)	71 (59)	85 (60)	89 (60)	57 (49)	86 (56)
Cardiovascular disease, no. (%)[1]	41 (24)	28 (23)	36 (26)	37 (25)	28 (24)	30 (19)
Fracture, no. (%)	16 (9)	14 (12)	13 (9)	12 (8)	9 (8)	8 (5)
Screening eGFR original, mL/min/1.73 m^2, mean (SD)	72 (9)	83 (9)	52 (4)	60 (5)	37 (4)	44 (5)
Screening eGFR recalculated, mL/min/1.73 m^2, mean (SD)	62 (8)	72 (8)	45 (4)	52 (4)	32 (4)	38 (4)
Screening UACR, mg/g, median (IQR)	488 (178-1022)	462 (185-883)	573 (293-1273)	565 (227-1273)	665 (296-1739)	511 (241-1277)
Albuminuria, no (%)						
Normal	13 (7)	13 (11)	9 (6)	12 (8)	6 (5)	7 (5)
Microalbuminuria	46 (26)	31 (26)	28 (20	30 (20)	26 (22)	44 (29)
Macroalbuminuria	115 (66)	76 (63)	104 (74)	107 (72)	85 (73)	103 (67)
Drug therapy, no. (%)						
Insulin	72 (41)	38 (32)	55 (39)	70 (47)	46 (39)	49 (32)
Sulfonylurea	19 (11)	16 (13)	19 (13)	12 (8)	24 (21)	27 (18)
Metformin	51 (29)	35 29)	36 (26)	38 (26)	20 (17)	27 (18)
GLP-1 receptor agonist	7 (4)	4 (3)	4 (3)	6 (4)	5 (4)	3 (2)
Statin	49 (28)	26 (22)	53 (38)	54 (36)	47 (40)	50 (32)
Antithrombotic[1]	45 (26)	27 (23)	41 (29)	45 (30)	40 (34)	40 (26)
RAAS inhibitor	88 (51)	51 (43)	73 (52)	80 (54)	61 (52)	69 (45)
β-Blocker	29 (17)	15 (13)	36 (26)	39 (26)	35 (30)	32 (21)
Diuretic	55 (32)	30 (25)	36 (26)	47 (32)	47 (40)	44 (29)

SD, standard deviation; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; IQR, interquartile range; GLP-1, glucagon-like peptide-1; RAAS, renin-angiotensin-aldosterone system.

[1]Includes antiplatelets and anticoagulants.

Supplemental Table 6. Event rates and effect estimates for primary composite, cardiovascular and kidney endpoints before and after recalculation of screening eGFR according to the 2009 CKD-EPI equation with and without a race-specific coefficient.

Endpoint	eGFR Group mL/min/1.73m^2	Events no./ Total Patients no.			Incidence Rate		Hazard ratio (95% CI)	P[1]
		Total	CANA	Placebo	CANA	Placebo		
Primary composite		585/4401	245/2202	340/2199	43.2	61.2	0.70 (0.59-0.82)	
	Original							0.19
	≥60 to <90	156/1820	70/913	86/907	29.5	36.8	0.80 (0.58-1.10)	
	≥45 to <60	158/1278	57/640	101/638	34.1	62.4	0.54 (0.39-0.75)	
	≥30 to <45	271/1303	118/649	153/654	72.4	95.8	0.74 (0.59-0.95)	
	Recalculated							0.30
	≥60 to <90	150/1783	67/894	83/889	28.9	36.3	0.79 (0.57-1.09)	
	≥45 to <60	160/1286	58/644	102/642	34.6	62.5	0.55 (0.40-0.75)	
	≥30 to <45	267/1310	115/652	152/658	70.0	94.3	0.73 (0.57-0.93)	
	<30	8/22	5/12	3/10	170.9	125.7	1.54 (0.37-6.45)	
Kidney Failure		281/4401	116/2202	165/2199	20.4	29.4	0.68 (0.54-0.86)	
	Original							0.19
	≥60 to <90	33/1820	16/913	17/907	6.7	7.2	0.93 (0.47-1.84)	
	≥45 to <60	68/1278	22/640	46/638	13.1	28	0.47 (0.28-0.77)	
	≥30 to <45	180/1303	78/649	102/654	47.8	63.4	0.74 (0.55-0.98)	
	Recalculated							0.24
	≥60 to <90	30/1783	15/894	15/889	6.4	6.5	0.99 (0.48-2.02)	
	≥45 to <60	68/1286	21/644	47/642	12.5	28.4	0.44 (0.26-0.73)	
	≥30 to <45	177/1310	77/652	100/658	46.8	61.5	0.75 (0.56-1.01)	
	<30	6/22	3/12	3/10	102.2	125.7	0.94 (0.19-4.67)	
Doubling of serum creatinine		306/4401	118/2202	188/2199	20.7	33.8	0.60 (0.48-0.76)	
	Original							0.13
	≥60 to <90	70/1820	33/913	37/907	13.9	15.9	0.87 (0.55-1.40)	
	≥45 to <60	91/1278	29/640	62/638	17.4	38.3	0.45 (0.29-0.69)	
	≥30 to <45	145/1303	56/649	89/654	33.9	55.2	0.60 (0.43-0.84)	
	Recalculated							0.23
	≥60 to <90	67/1783	32/894	35/889	13.8	15.3	0.89 (0.55-1.44)	
	≥45 to <60	91/1286	29/644	62/642	17.3	38.0	0.45 (0.29-0.70)	
	≥30 to <45	143/1310	55/652	88/658	33.0	54.1	0.60 (0.43-0.84)	
	<30	5/22	2/12	3/10	65.2	124.0	0.64 (0.11-3.82)	
Kidney Composite		377/4401	153/2202	224/2199	27.0	40.4	0.66 (0.53-0.81)	
	Original							0.19
	≥60 to <90	75/1820	35/913	40/907	14.8	17.1	0.86 (0.55-1.35)	
	≥45 to <60	103/1278	35/640	68/638	21	42	0.49 (0.33-0.74)	
	≥30 to <45	199/1303	83/649	116/654	50.9	72.6	0.69 (0.52-0.91)	
	Recalculated							0.29
	≥60 to <90	72/1783	34/894	38/889	14.7	16.7	0.87 (0.55-1.39)	
	≥45 to <60	102/1286	34/644	68/642	20.3	41.7	0.48 (0.32-0.73)	

	≥30 to <45	197/1310	82/652	115/658	49.9	71.3	0.69 (0.52-0.91)	
	<30	6/22	3/12	3/10	102.6	125.7	0.94 (0.19-4.67)	
HHF	**All**	230/4401	89/2202	141/2199	15.7	25.3	0.61 (0.47-0.80)	
	Original							0.47
	≥60 to <90	69/1820	28/913	41/907	11.8	17.6	0.67 (0.41-1.08)	
	≥45 to <60	72/1278	24/640	48/638	14.4	30.0	0.48 (0.29-0.78)	
	≥30 to <45	89/1303	37/649	52/654	22.4	31.7	0.70 (0.46-1.07)	
	Recalculated							0.74
	≥60 to <90	67/1783	28/894	39/889	12.1	17.2	0.70 (0.43-1.14)	
	≥45 to <60	71/1286	24/644	47/642	14.4	29.1	0.50 (0.30-0.81)	
	≥30 to <45	91/1310	37/652	54/658	22.2	32.7	0.67 (0.44-1.02)	
	<30	1/22	0/12	1/10	0	41.1	NA	
CV death		250/4401	110/2202	140/2199	19	24.4	0.78 (0.61-1.00)	
	Original							0.82
	≥60 to <90	86/1820	38/913	48/907	15.8	20.2	0.78 (0.51-1.20)	
	≥45 to <60	68/1278	28/640	40/638	16.6	24.0	0.69 (0.43-1.12)	
	≥30 to <45	96/1303	44/649	52/654	26	30.6	0.85 (0.57-1.26)	
	Recalculated							0.99
	≥60 to <90	83/1783	36/894	47/889	15.3	20.3	0.75 (0.49-1.16)	
	≥45 to <60	71/1286	30/644	41/642	17.7	24.3	0.72 (0.45-1.15)	
	≥30 to <45	94/1310	42/652	52/658	24.6	30.4	0.81 (0.54-1.21)	
	<30	2/22	2/12	0/10	61.8	0	NA	
All-cause mortality		369/4401	168/2202	201/2199	29.0	35.0.	0.83 (0.68-1.02)	
	Original							0.38
	≥60 to <90	132/1820	63/913	69/907	26.2	29.1	0.90 (0.64-1.27)	
	≥45 to <60	103/1278	41/640	62/638	24.3	37.1	0.66 (0.44-0.97)	
	≥30 to <45	134/1303	64/649	70/654	37.8	41.3	0.91 (0.65-1.28)	
	Recalculated							0.89
	≥60 to <90	128/1783	60/894	68/889	25.5	29.3	0.87 (0.61-1.23)	
	≥45 to <60	105/1286	44/644	61/642	25.9	36.2	0.71 (0.48-1.05)	
	≥30 to <45	134/1310	62/652	72/658	36.4	42.1	0.86 (0.61-1.21)	
	<30	2/22	2/12	0/10	61.8	0	NA	

Incidence rate per 1000 patient years. CANA, canagliflozin; CI, confidence interval; HHF, hospitalized heart failure; CV, cardiovascular; NA, not applicable. [1]P-for trend across eGFR categories.

Supplemental Table 7. Event rates and effect estimates for primary composite, cardiovascular and kidney endpoints before and after recalculation of screening eGFR according to the 2009 CKD-EPI equation with and without a race-specific coefficient in Black Participants.

Endpoint	eGFR Group mL/min/1.73m^2	Events no./ Total Patients no.			Incidence Rate		Hazard Ratio (95% CI)	P-Value[1]
		Total	CANA	Placebo	CANA	Placebo		
Primary composite		37/224	18/112	19/112	60.5	64.4	0.82 (0.43-1.59)	
	Original							0.79
	≥60 to <90	12/89	5/42	7/47	47.6	57.0	0.67 (0.20-2.29)	
	≥45 to <60	8/73	3/37	5/36	28.6	50.1	0.57 (0.14-2.40)	
	≥30 to <45	17/62	10/33	7/29	114.2	96.5	1.20 (0.45-3.16)	
	Recalculated							0.91
	≥60 to <90	6/52	2/23	4/29	36.0	56.2	0.69 (0.13-3.75)	
	≥45 to <60	10/81	4/41	6/40	36.0	53.2	0.65 (0.18-2.33)	
	≥30 to <45	13/69	7/36	6/33	69.1	68.7	0.89 (0.30-2.67)	
	<30	8/22	5/12	3/10	170.9	125.6	1.54 (0.37-4.45)	
Kidney Failure		19/224	10/112	9/112	33.6	30.3	0.91 (0.37-2.26)	
	Original							0.79
	≥60 to <90	3/89	1/42	2/47	9.5	16.2	0.56 (0.05-6.15)	
	≥45 to <60	3/73	2/37	1/36	19.1	9.9	1.93 (0.18-21.25)	
	≥30 to <45	13/62	7/33	6/29	79.8	82.4	0.93 (0.31-2.81)	
	Recalculated							0.79
	≥60 to <90	0/52	0/23	0/29	0.0	0.0	NA	
	≥45 to <60	3/81	1/41	2/40	9.0	17.6	0.49 (0.05-5.45)	
	≥30 to <45	10/69	6/36	4/33	59.1	45.4	1.18 (0.33-4.21)	
	<30	6/22	3/12	3/10	102.2	125.7	0.94 (0.19-4.67)	
Doubling of serum creatinine		16/224	6/112	10/112	19.9	33.6	0.52 (0.19-1.45)	
	Original							0.71
	≥60 to <90	3/89	1/42	2/47	9.5	16.3	0.60 (0.05-6.57)	
	≥45 to <60	5/73	1/37	4/36	9.5	40.0	0.25 (0.03-2.21)	
	≥30 to <45	8/62	4/33	4/29	43.9	53.5	0.79 (0.20-3.20)	
	Recalculated							
	≥60 to <90	0/52	0/23	0/29	0.0	0.0	NA	0.72
	≥45 to <60	5/81	1/41	4/40	9.0	35.5	0.28 (0.03-2.54)	
	≥30 to <45	6/69	3/36	3/33	29.0	33.6	0.74 (0.15-3.68)	
	<30	5/22	2/12	3/10	65.2	124.1	0.64 (0.11-3.82)	
Kidney Composite		22/224	10/112	12/112	33.6	40.7	0.72 (0.31-1.68)	
	Original							0.85
	≥60 to <90	3/89	1/42	2/47	9.5	16.3	0.60 (0.05-6.57)	
	≥45 to <60	6/73	2/37	4/36	19.1	40.0	0.48 (0.09-2.60)	
	≥30 to <45	13/62	7/33	6/29	79.9	82.7	0.98 (0.33-2.92)	
	Recalculated							0.60
	≥60 to <90	0/52	0/23	0/29	0.0	0.0	NA	

	≥45 to <60	5/81	1/41	4/40	9.0	35.5	0.28 (0.03-2.54)	
	≥30 to <45	11/69	6/36	5/33	59.2	57.3	0.91 (0.28-3.01)	
	<30	6/22	3/12	3/10	102.6	125.7	0.94 (0.19-4.67)	
HHF		19/224	6/112	13/112	20.1	45.2	0.46 (0.17-1.21)	
	Original							0.80
	≥60 to <90	6/89	1/42	5/47	9.4	41.6	0.23 (0.03-1.97)	
	≥45 to <60	8/73	3/37	5/36	29.6	53.5	0.55 (0.13-2.30)	
	≥30 to <45	5/62	2/33	3/29	22.0	40.6	0.44 (0.07-2.77)	
	Recalculated							0.89
	≥60 to <90	4/52	1/23	3/29	18.2	44.9	0.43 (0.05-4.17)	
	≥45 to <60	7/81	3/41	4/40	27.7	35.7	0.78 (0.17-3.48)	
	≥30 to <45	7/69	2/36	5/33	19.5	59.2	0.31 (0.06-1.59)	
	<30	1/22	0/12	1/10	0.0	41.1	NA	
CV death		15/224	8/112	7/112	26.2	22.9	1.03 (0.36-2.96)	
	Original							0.76
	≥60 to <90	9/89	4/42	5/47	37.5	39.7	0.71 (0.17-2.98)	
	≥45 to <60	2/73	1/37	1/36	9.4	9.9	0.95 (0.06-15.12)	
	≥30 to <45	4/62	3/33	1/29	32.1	12.7	2.53 (0.26-24.41)	
	Recalculated							0.95
	≥60 to <90	6/52	2/23	4/29	36.0	56.2	0.69 (0.13-3.75)	
	≥45 to <60	5/81	3/41	2/40	26.6	17.2	1.23 (0.20-7.59)	
	≥30 to <45	2/69	1/36	1/33	9.5	10.9	0.79 (0.05-12.64)	
	<30	2/22	2/12	0/10	61.8	0.0	NA	
All-cause mortality		22/224	12/112	10/112	39.2	28.5	1.13 (0.48-2.67)	
	Original							0.23
	≥60 to <90	12/89	7/42	5/47	65.7	39.7	1.41 (0.43-4.61)	
	≥45 to <60	5/73	1/37	4/36	9.4	39.5	0.24 (0.03-2.15)	
	≥30 to <45	5/62	4/33	1/29	42.8	12.7	3.21 (0.36-28.88)	
	Recalculated							0.89
	≥60 to <90	8/52	4/23	4/29	71.9	56.2	1.35 (0.34-5.41)	
	≥45 to <60	7/81	4/41	3/40	35.5	25.7	1.20 (0.26-5.52)	
	≥30 to <45	5/69	2/36	3/33	19.0	32.8	0.52 (0.09-3.13)	
	<30	2/22	2/12	0/10	61.8	0.0	NA	

Incidence rate per 1000 patient years. CANA, canagliflozin; CI, confidence interval; HHF, hospitalized heart failure; CV, cardiovascular; NA, not applicable. [1]P value for trend across eGFR categories.

Supplemental Table 8. Event rates and effect estimates for primary composite, cardiovascular and kidney endpoints before and after recalculation of screening eGFR according to the 2021 CKD-Epi equation in all and Black Participants.

	eGFR Group	Events no./Total Patients no.			Incidence Rate		Hazard ratio	P[1]
Endpoint	mL/min/1.73m^2	Total	CANA	Placebo	CANA	Placebo	(95% CI)	
Primary composite	All	585/4401	245/2202	340/2199	43.2	61.2	0.70 (0.59-0.82)	
	Original							0.19
	≥60 to <90	156/1820	70/913	86/907	29.5	36.8	0.80 (0.58-1.10)	
	≥45 to <60	158/1278	57/640	101/638	34.1	62.4	0.54 (0.39-0.75)	
	≥30 to <45	271/1303	118/649	153/654	72.4	95.8	0.74 (0.59-0.95)	
	Recalculated							0.56
	≥60	178/2069	75/1036	103/1033	27.7	38.7	0.71 (0.53-0.96)	
	≥45 to <60	158/1233	61/612	97/621	38.6	61.5	0.62 (0.45-0.86)	
	≥30 to <45	240/1057	106/531	134/526	79.7	105.5	0.74 (0.57-0.96)	
	<30	8/38	2/20	6/18	41.8	147.3	0.28 (0.06-1.40)	
	Black	37/224	18/112	19/112	60.5	64.4	0.82 (0.43-1.59)	
	Original							0.79
	≥60 to <90	12/89	5/42	7/47	47.6	57.0	0.67 (0.20-2.29)	
	≥45 to <60	8/73	3/37	5/36	28.6	50.1	0.57 (0.14-2.40)	
	≥30 to <45	17/62	10/33	7/29	114.2	96.5	1.20 (0.45-3.16)	
	Recalculated							0.79
	≥60	8/70	4/33	4/37	49.3	42.1	1.21 (0.30-4.83)	
	≥45 to <60	9/79	3/40	6/39	26.1	54..9	0.49 (0.12-1.98)	
	≥30 to <45	19/66	11/36	8/30	120.1	105.9	1.11 (0.44-2.76)	
	<30	1/8	0/3	1/5	0	83.0	NA	
Kidney Composite	All	377/4401	153/2202	224/2199	27.0	40.4	0.66 (0.53-0.81)	
	Original							0.19
	≥60 to <90	75/1820	35/913	40/907	14.8	17.1	0.86 (0.55-1.35)	
	≥45 to <60	103/1278	35/640	68/638	21	42	0.49 (0.33-0.74)	
	≥30 to <45	199/1303	83/649	116/654	50.9	72.6	0.69 (0.52-0.91)	
	Recalculated							0.59
	≥60	86/2069	35/1036	51/1033	13.0	19.2	0.67 (0.43-1.03)	
	≥45 to <60	103/1233	39/612	64/621	24.7	40.6	0.60 (0.41-0.90)	
	≥30 to <45	181/1057	77/531	104/526	58.0	81.9	0.69 (0.51-0.93)	
	<30	6/38	1/20	5/18	20.9	122.7	0.17 (0.02-1.47)	
	Black	22/224	10/112	12/112	33.6	40.7	0.72 (0.31-1.68)	
	Original							0.85
	≥60 to <90	3/89	1/42	2/47	9.5	16.3	0.60 (0.05-6.57)	
	≥45 to <60	6/73	2/37	4/36	19.1	40.0	0.48 (0.09-2.60)	
	≥30 to <45	13/62	7/33	6/29	79.9	82.7	0.98 (0.33-2.92)	
	Recalculated							0.78
	≥60	1/70	1/33	0/37	12.3	0	NA	
	≥45 to <60	5/79	1/40	4/39	8.7	36.6	0.25 (0.03-2.27)	
	≥30 to <45	15/66	8/36	7/30	87.3	92.6	0.92 (0.33-2.53)	
	<30	1/8	0/3	1/5	0	83.0	NA	

Kidney Failure	All	281/4401	116/2202	165/2199	20.4	29.4	0.68 (0.54-0.86)	
	Original							0.19
	≥60 to <90	33/1820	16/913	17/907	6.7	7.2	0.93 (0.47-1.84)	
	≥45 to <60	68/1278	22/640	46/638	13.1	28	0.47 (0.28-0.77)	
	≥30 to <45	180/1303	78/649	102/654	47.8	63.4	0.74 (0.55-0.98)	
	Recalculated							0.32
	≥60	41/2069	19/1036	22/1033	7.0	8.2	0.85 (0.46-1.57)	
	≥45 to <60	67/1233	22/612	45/621	13.8	28.2	0.49 (0.30-0.82)	
	≥30 to <45	167/1057	73/531	94/526	54.8	73.5	0.73 (0.54-0.99)	
	<30	5/38	1/20	4/18	20.9	97.4	0.22 (0.02-1.94)	
	Black	19/224	10/112	9/112	33.6	30.3	0.91 (0.37-2.26)	
	Original							0.79
	≥60 to <90	3/89	1/42	2/47	9.5	16.2	0.56 (0.05-6.15)	
	≥45 to <60	3/73	2/37	1/36	19.1	9.9	1.93 (0.18-21.25)	
	≥30 to <45	13/62	7/33	6/29	79.8	82.4	0.93 (0.31-2.81)	
	Recalculated							0.95
	≥60	1/70	1/33	0/37	12.3	0	NA	
	≥45 to <60	3/79	1/40	2/39	8.7	18.1	0.48 (0.04-5.28)	
	≥30 to <45	14/66	8/36	6/30	87.1	78.6	1.10 (0.38-3.17)	
	<30	1/8	0/3	1/5	0	83.0	NA	
Doubling of serum creatinine	All	306/4401	118/2202	188/2199	20.7	33.8	0.60 (0.48-0.76)	
	Original							0.13
	≥60 to <90	70/1820	33/913	37/907	13.9	15.9	0.87 (0.55-1.40)	
	≥45 to <60	91/1278	29/640	62/638	17.4	38.3	0.45 (0.29-0.69)	
	≥30 to <45	145/1303	56/649	89/654	33.9	55.2	0.60 (0.43-0.84)	
	Recalculated							0.74
	≥60	80/2069	33/1036	47/1033	12.2	17.7	0.68 (0.44-1.06)	
	≥45 to <60	89/1233	32/612	57/621	20.2	36.1	0.56 (0.36-0.86)	
	≥30 to <45	131/1057	51/531	80/526	37.7	62.5	0.58 (0.41-0.83)	
	<30	5/38	1/20	4/18	20.9	92.9	0.24 (0.03-2.15)	
	Black	16/224	6/112	10/112	19.9	33.6	0.52 (0.19-1.45)	
	Original							0.71
	≥60 to <90	3/89	1/42	2/47	9.5	16.3	0.60 (0.05-6.57)	
	≥45 to <60	5/73	1/37	4/36	9.5	40.0	0.25 (0.03-2.21)	
	≥30 to <45	8/62	4/33	4/29	43.9	53.5	0.79 (0.20-3.20)	
	Recalculated							-
	≥60	1/70	1/33	0/37	12.3	0	NA	
	≥45 to <60	4/79	0/40	4/39	0	36.6	NA	
	≥30 to <45	10/66	5/36	5/30	52.6	64.2	NA	
	<30	1/8	0/3	1/5	0	83.0	NA	
HHF	All	230/4401	89/2202	141/2199	15.7	25.3	0.61 (0.47-0.80)	
	Original							0.47
	≥60 to <90	69/1820	28/913	41/907	11.8	17.6	0.67 (0.41-1.08)	
	≥45 to <60	72/1278	24/640	48/638	14.4	30.0	0.48 (0.29-0.78)	

	≥30 to <45	89/1303	37/649	52/654	22.4	31.7	0.70 (0.46-1.07)	
	Recalculated							0.89
	≥60	84/2069	32/1036	52/1033	11.9	19.7	0.60 (0.39-0.93)	
	≥45 to <60	67/1233	24/612	43/621	15.2	27.4	0.55 (0.34-0.91)	
	≥30 to <45	77/1057	33/531	44/526	24.3	33.6	0.72 (0.46-1.13)	
	<30	2/38	0/20	2/18	0	45.5	NA	
	Black	19/224	6/112	13/112	20.1	45.2	0.46 (0.17-1.21)	
	Original							0.80
	≥60 to <90	6/89	1/42	5/47	9.4	41.6	0.23 (0.03-1.97)	
	≥45 to <60	8/73	3/37	5/36	29.6	53.5	0.55 (0.13-2.30)	
	≥30 to <45	5/62	2/33	3/29	22.0	40.6	0.44 (0.07-2.77)	
	Recalculated							0.82
	≥60	5/70	1/33	4/37	12.2	44.7	0.29 (0.03-2.58)	
	≥45 to <60	9/79	4/40	5/39	36.3	47.2	0.79 (0.21-2.94)	
	≥30 to <45	4/66	1/36	3/30	10.4	38.3	0.24 (0.02-2.32)	
	<30	1/8	0/3	1/5	0	92.1	NA	
CV death	All	250/4401	110/2202	140/2199	19	24.4	0.78 (0.61-1.00)	
	Original							0.82
	≥60 to <90	86/1820	38/913	48/907	15.8	20.2	0.78 (0.51-1.20)	
	≥45 to <60	68/1278	28/640	40/638	16.6	24.0	0.69 (0.43-1.12)	
	≥30 to <45	96/1303	44/649	52/654	26	30.6	0.85 (0.57-1.26)	
	Recalculated							0.97
	≥60	98/2069	42/1036	56/1033	15.4	20.7	0.74 (0.50-1.11)	
	≥45 to <60	68/1233	29/612	39/621	18.1	23.9	0.75 (0.47-1.22)	
	≥30 to <45	82/1057	38/531	44/526	27.4	32.4	0.84 (0.54-1.29)	
	<30	2/38	1/20	1/18	20.8	21.2	0.87 (0.05-13.88)	
	Black	15/224	8/112	7/112	26.2	22.9	1.03 (0.36-2.96)	
	Original							0.76
	≥60 to <90	9/89	4/42	5/47	37.5	39.7	0.71 (0.17-2.98)	
	≥45 to <60	2/73	1/37	1/36	9.4	9.9	0.95 (0.06-15.12)	
	≥30 to <45	4/62	3/33	1/29	32.1	12.7	2.53 (0.26-24.41)	
	Recalculated							0.91
	≥60	7/70	3/33	4/37	36.3	42.1	0.92 (0.21-4.09)	
	≥45 to <60	4/79	2/40	2/39	17.4	17.7	0.98 (0.14-6.97)	
	≥30 to <45	4/66	3/36	1/30	30.5	12.3	2.41 (0.25-23.25)	
	<30	0/8	0/3	0/5	0	0	NA	
All-cause mortality	All	369/4401	168/2202	201/2199	29.0	35.0.	0.83 (0.68-1.02)	
	Original							0.38
	≥60 to <90	132/1820	63/913	69/907	26.2	29.1	0.90 (0.64-1.27)	
	≥45 to <60	103/1278	41/640	62/638	24.3	37.1	0.66 (0.44-0.97)	
	≥30 to <45	134/1303	64/649	70/654	37.8	41.3	0.91 (0.65-1.28)	
	Recalculated							0.34
	≥60	149/2069	70/1036	79/1033	25.6	29.2	0.87 (0.63-1.21)	
	≥45 to <60	103/1233	39/612	64/621	24.3	39.3	0.62 (0.42-0.92)	
	≥30 to <45	114/1057	57/531	57/526	41.1	42.0	0.97 (0.67-1.40)	

<30	3/38	2/20	1/18	41.6	21.2	1.76 (0.16-19.38)	
Black	22/224	12/112	10/112	39.2	28.5	1.13 (0.48-2.67)	
Original							0.23
≥60 to <90	12/89	7/42	5/47	65.7	39.7	1.41 (0.43-4.61)	
≥45 to <60	5/73	1/37	4/36	9.4	39.5	0.24 (0.03-2.15)	
≥30 to <45	5/62	4/33	1/29	42.8	12.7	3.21 (0.36-28.88)	
Recalculated							0.72
≥60	10/70	6/33	4/37	72.6	42.1	1.79 (0.51-6.36)	
≥45 to <60	6/79	2/40	4/39	17.4	35.3	0.51 (0.09-2.81)	
≥30 to <45	6/66	4/36	2/30	40.6	24.6	1.60 (0.29-8.74)	
<30	0/8	0/3	0/5	0	0	NA	

Incidence rate per 1000 patient years. CANA, canagliflozin; CI, confidence interval; NA, not applicable. [1]P value for trend across eGFR categories.

Supplemental Table 9. Annual eGFR decline and treatment effect estimates for Black participants after recalculation of screening eGFR (2009 CKD-Epi) and exclusion of individuals not meeting inclusion criteria following eGFR recalculation (2009 CKD-Epi).

	CANA Mean (95% CI), mL/min/1.73m^2	**P**[1]	**Placebo** Mean (95% CI), mL/min/1.73m^2	**P**[1]	**Treatment Effect** Mean (SE), mL/min/1.73m^2	95% CI	P-value
Recalculated eGFR (2009 CKD-Epi)							
Acute Phase	-3.47 (-3.84, -3.10)	<0.0001	-0.53 (-0.90, -0.16)	0.005	-2.94 (0.27)	(-3.46, -2.42)	<0.0001
Black	-3.57 (-5.08, -2.06)	<0.0001	-0.22 (-1.64, 1.21)	0.76	-3.35 (1.05)	(-5.42, -1.28)	0.002
Other	-3.47 (-3.85, -3.09)	<0.0001	-0.54 (-0.92, -0.16)	0.005	-2.93 (0.27)	(-3.46, -2.39)	<0.0001
Chronic Phase	-1.89 (-2.14, -1.64)	<0.0001	-4.58 (-4.83, -4.32))	<0.0001	2.68 (0.18)	(2.32, 3.04)	<0.0001
Black	-2.10 (-3.15, -1.05))	0.0001	-4.62 (-5.66, -3.58)	<0.0001	2.52 (0.75)	(1.04, 3.99)	0.001
Other	-1.88 (-2.14, -1.62)	<0.0001	-4.57 (-4.84, -4.31)	<0.0001	2.69 (0.19)	(2.32, 3.06)	<0.0001
Total Slope	-3.14 (-3.41, -2.87)	<0.0001	-4.70 (-4.97, -4.42)	<0.0001	1.56 (0.20)	(1.18, 1.95)	<0.0001
Black	-3.35 (-4.45, -2.25)	<0.0001	-4.80 (-5.87, -3.72)	<0.0001	1.44 (0.78)	(-0.09, 2.98)	0.07
Other	-3.13 (-3.40, -2.85)	<0.0001	-4.69 (-4.97, -4.41)	<0.0001	1.57 (0.20)	(1.17, 1.96)	<0.0001

CANA, canagliflozin; CI, confidence interval; SE, standard error; Acute phase, baseline to week 3; Chronic phase, week 3 to week 130 during the trial. Effects on eGFR slope were estimated by a piecewise linear mixed-effect model using an intention-to treat approach.

[1]Compared with baseline.

Supplemental Table 10. Annual eGFR decline and treatment effect estimates for randomized participants after recalculation of screening eGFR (2021 CKD-Epi) and exclusion of individuals not meeting inclusion criteria following eGFR recalculation (2021 CKD-Epi).

	CANA Mean (95% CI), mL/min/1.73m^2	**P**[1]	**Placebo** Mean (95% CI), mL/min/1.73m^2	**P**[1]	**Treatment Effect** Mean (SE), mL/min/1.73m^2	95% CI	P-value
			Recalculated eGFR (2021 CKD-Epi)				
Acute Phase	-3.15 (-3.53, -2.77)	<0.0001	-0.44 (-0.82, -0.06)	0.02	-2.71 (0.28)	(-3.25, -2.17)	<0.0001
Black	-3.80 (-5.24, -2.35)	<0.0001	0.17 (-1.27, 1.61)	0.82	-3.96 (1.04)	(-6.00, -1.93)	0.001
Other	-3.12 (-3.52, -2.73)	<0.0001	-0.46 (-0.86, -0.07)	0.02	-2.66 (0.28)	(-3.22, -2.10)	<0.0001
Chronic Phase	-1.68 (-1.95, -1.40)	<0.0001	-4.39 (-4.67, -4.11)	<0.0001	2.72 (0.20)	(2.33, 3.11)	<0.0001
Black	-2.14 (-3.23, -1.05))	0.0002	-4.64 (-5.74, -3.54)	<0.0001	2.50 (0.78)	(0.96, 4.05)	0.002
Other	-1.65 (-1.93, -1.37)	<0.0001	-4.38 (-4.66, -4.09)	<0.0001	2.73 (0.21)	(2.32, 3.13)	<0.0001
Total Slope	-2.78 (-3.07, -2.50)	<0.0001	-4.46 (-4.75, -4.17)	<0.0001	1.68 (0.21)	(1.27, 2.09)	<0.0001
Black	-3.50 (-4.58, -2.43)	<0.0001	-4.66 (-5.74, -3.58)	<0.0001	1.16 (0.77)	(-0.37, 2.68)	0.14
Other	-2.75 (-3.04, -2.45)	<0.0001	-4.45 (-4.75, -4.15)	<0.0001	1.70 (0.21)	(1.28, 2.12)	<0.0001

CANA, canagliflozin; CI, confidence interval; SE, standard error; Acute phase, baseline to week 3; Chronic phase, week 3 to week 130 during the trial. Effects on eGFR slope were estimated by a piecewise linear mixed-effect model using an intention-to treat approach.

[1]Compared with baseline.