Inclusion criteria	1) Written informed consent must be provided before participation. Patient information and consent form must be approved by relevant independent EC. Specifically, all participating patients will be asked to give informed consent for long-term follow-up and collection of follow-up data 2) Male or female patients ≥ 18 years and < 75 years of age at Screening visit 3) Type 2 DM (WHO criteria) 4) Persistent normoalbuminuria (at least 2 of 3 UACR < 30 mg/g samples from ”run in”-period) 5) eGFR >45 ml/min/1.73m^2 at Screening visit 6) The patient must be willing and able to comply with the protocol for the duration of the study 7) Female without child-bearing potential at the screening visit. Defined as one or more of following: 7.1) Female patients ≥ 50 years of age at the day of inclusion, who have been postmenopausal for at least 1 year 7.2) Female patients < 50 years of age at the day of inclusion, who have been postmenopausal for at least 1 year and serum FSH levels > 40 mIU/mL as well as serum estrogen levels < 30 pg/ml or a negative estrogen test. 7.3) 6 weeks after surgical sterilization by bilateral tubal ligation or bilateral ovariectomy with or without hysterectomy. OR a negative urine pregnancy test at the Screening visit AND one or more of following: 7.4) Correct use of reliable contraception methods. This includes one or more of the following: hormonal contraceptive (such as injection, transdermal patch, implant, cervical ring or oral) or an intrauterine device (IUD) OR correct use of double barrier with one of the following: barrier methods (diaphragm, cervical cap, Lea contraceptive, femidom or condom) AND in combination with a spermicide. 7.5) General sexual abstinence from the time of screening/ baseline, during the study until a minimum of 30 days after the last administration of study medication if this is already established as the patient’s preferred and usual lifestyle. 7.6) Having only female sexual partners.

	7.7) Sexual relationship with sterile male partners only
Exclusion criteria	1) Average of systolic BP< 110 or >160 mm Hg at baseline 2) Average of diastolic BP > 100 mm Hg at baseline 3) Type 1 DM (WHO criteria) 4) HbA1c <6.5% (48 mmo l/ mol) AND > 5 years of known duration of diabetes type 2 AND never treated with an antidiabetic drug of any kind. 5) Current in treatment with more than one RAAS blocking agent (Angiotensin Converting Enzyme inhibitor, Angiotensin Receptor Blocker or Direct Renin Inhibitor) 6) Current lithium treatment(ATC: N05AN) 7) Known or suspected hypersensitivity to Spironolactone or to any of its excipients. 8) Current use of potassium sparing diuretics (ATC: C03D, C03E), such as: Spironolactone, Eplerenone or Amiloride etc. 9) Hyperkalemia at Screening: plasma potassium level >5.0 mmol/L or serum potassium level >5.4 mmol/L. 10) Hyponatriemia determine by the investigator 11) Current cancer treatment or within five years from baseline (except basal cell skin cancer or squamous cell skin cancer) 12) Any clinically significant disorder, except for conditions associated with type 2 DM history, which in the Investigators opinion could interfere with the results of the trial 13) Cardiac disease defined as: Heart failure (NYHA class III-IV) and/or diagnosis of unstable angina pectoris and/or MI, stroke, PTCA or CABG within the last 3 months 14) Diagnosis of non-Diabetic CKD current or in the past 15) Diagnosis of liver cirrhosis with current impaired liver function within the last 3 years. 16) Diagnosis of Addison's disease. 17) Being lactating. 18) Intend to become pregnant within the duration of the study or not use adequate birth control. 19) Known or suspected abuse of alcohol or narcotics 20) Not able to understand informed consent form 21) Participation in any other intervention trial than PRIORITY or a related sub-study is not allowed within 30 days before inclusion or concurrent to this study

Supplementary Table 1: A complete list of inclusion and exclusion criteria in the PRIORITY study.

Variables	CKD273 high risk No Retinopathy	CKD273 high risk Retinopathy	p	CKD273 low risk No retinopathy	CKD273 low risk Retinopathy	p
N	175	41		1279	263	
Age, years	63.2 (6.7)	63.3 (5.7)	0.960	61.2 (8.5)	62.7 (8.0)	0.009
Male, n (%)	115 (65.7)	34 (82.9)	0.050	784 (61)	164 (62.4)	0.801
Non-White, n (%)	2 (1.1)	2 (4.9)	0.340	44 (3.4)	12 (4.6)	0.481
Diabetes duration, years	12.7 (7.9)	17.7 (8.7)	<0.001	10.2 (6.8)	17.7 (8.3)	<0.001
Retinopathy grade, n (%)			N/A			N/A
Non-proliferative	-	31 (77.5)		-	200 (76.3)	
Proliferative	-	8 (20.0)		-	48 (18.3)	
Maculopathy, n (%)	-	10 (24.4)		-	69 (27.2)	
History of laser therapy, n (%)	-	10 (25.6)		-	66 (25.8)	
HbA1c, mmol/mol	58 (13)	62 (14)	0.075	56 (11)	62 (12)	<0.001
eGFR ml/min/1.73m2	82 (17)	79 (18)	0.208	88 (15)	86 (16)	0.031
UACR, mg/g	7 [4, 11]	10 [6, 14]	0.007	5 [3, 8]	6 [4, 9]	0.007
CKD273, arbitrary unit	0.34 (0.17)	0.34 (0.17)	0.913	-0.44 (0.34)	-0.36 (0.30)	<0.001
Systolic BP, mmHg	136 (12)	132 (14)	0.134	133 (12)	134 (12)	0.628
Diastolic BP, mmHg	79 (9)	76 (9)	0.024	79 (8)	76 (10)	<0.001
BMI, kg/m2	30.7 (5.1)	31.2 (6.7)	0.560	30.3 (5.0)	30.5 (5.0)	0.628
LDL cholesterol, mmol/l	2.43 (1.08)	2.29 (0.84)	0.441	2.45 (0.92)	2.21 (0.83)	<0.001
Smoker, n (%)	81 (46.3)	16 (39.0)	0.505	575 (45.1)	110 (42.1)	0.420
RAAS-inhibitor treatment, n (%)	152 (86.9)	39 (95.1)	0.223	757 (59.2)	193 (73.4)	<0.001
Metformin treatment, n (%)	145 (83.3)	37 (90.2)	0.388	947 (77.9)	203 (78.1)	1.000
Insulin treatment, n (%)	51 (29.3)	22 (53.7)	0.005	314 (25.8)	145 (55.8)	<0.001
GLP1-RA treatment, n (%)	30 (17.2)	7 (17.1)	1.000	170 (14.0)	64 (24.6)	<0.001
SGLT2 inhibitor treatment, n (%)	13 (7.5)	7 (17.1)	0.108	78 (6.4)	23 (8.8)	0.203
History of IHD, n (%)	26 (14.9)	10 (24.4)	0.214	131 (10.2)	48 (18.3)	<0.001
History of stroke, n (%)	12 (6.9)	1 (2.4)	0.480	50 (3.9)	12 (4.6)	0.750

Supplementary Table 2: Baseline characteristics stratified by presence of diabetic retinopathy (DR) and CKD273 risk status at baseline. Data are presented as mean (standard deviation), median [inter-quartile range], or n (%). P-values were calculated using Student's t-test, Kruskal-Wallis rank sum test, and the $\chi 2$-test for continuous, non-normal continuous, and categorical variables, respectively. HbA1c: glycated hemoglobin; eGFR: estimated glomerular filtration rate; UACR: urinary albumin-creatinine rate; CKD273: urinary proteomics classifier; BP: blood pressure, BMI: body mass index, RAAS: renin-angiotensin-aldosterone system; GLP1-RA: glucagon like peptide 1 receptor agonist; SGLT2: sodium-glucose co-transporter 2; IHD: ischemic heart disease.

Variables	No DR	DR	p
N	1373	274	
Age, years	61.15 (8.38)	62.24 (7.85)	0.047
Male, n (%)	854 (62)	182 (66)	0.210
Non-White	43 (3)	13 (5)	0.245
Diabetes duration, years	10.33 (6.80)	17.47 (8.49)	<0.001
Low-risk CKD273 pattern, n (%)	1219 (89)	240 (88)	0.644
Retinopathy grade, n (%)			N/A
Non-proliferative	-	207 (76)	
Proliferative	-	51 (19)	
Maculopathy, n (%)	-	72 (27)	
History of laser therapy, n (%)	-	66 (25)	
HbA1c, mmol/mol	56 (12)	62 (13)	<0.001
HbA1c, %	7.3 (1.1)	7.8 (1.2)	<0.001
eGFR, mL/min/1.73m^2	89 (14)	88 (13)	0.210
UACR, mg/g	5 [3, 8]	6 [4, 10]	<0.001
CKD273, arbitrary unit	-0.36 (0.41)	-0.28 (0.37)	0.004
Systolic BP, mmHg	133 (12)	134 (12)	0.124
Diastolic BP, mmHg	79 (8)	76 (10)	<0.001
BMI, kg/m2	30.3 (5.0)	30.4 (5.2)	0.611
LDL, mmol/l	2.45 (0.94)	2.22 (0.83)	<0.001
Smoker, n (%)	619 (45)	117 (43)	0.549
RAAS-inhibitor treatment, n (%)	846 (62)	205 (75)	<0.001
Metformin treatment, n (%)	1041 (79)	221 (82)	0.397
Insulin treatment, n (%)	343 (26)	142 (52)	<0.001
GLP1-RA treatment, n (%)	184 (14)	65 (24)	<0.001
SGLT2-inhibitor treatment, n (%)	83 (6)	27 (10)	0.042
History of IHD, n (%)	145 (11)	51 (19)	<0.001
History of stroke, n (%)	56 (4)	11 (4)	1.000

Supplementary Table 3: Baseline characteristics for all participants with estimated glomerular filtration rate (eGFR) >60 mL/min/1.73m^2 at baseline, stratified by presence of diabetic retinopathy (DR) at baseline. Data are presented as mean (standard deviation), median [inter-quartile range], or n (%). P-values were calculated using Student's t-test, Kruskal-Wallis rank sum test, and the χ2-test for continuous, non-normal continuous, and categorical variables, respectively. HbA1c: glycated hemoglobin; UACR: urinary albumin-creatinine rate; CKD273: urinary proteomics classifier; BP: blood pressure, BMI: body mass index, RAAS: renin-angiotensin-aldosterone system; GLP1-RA: glucagon like peptide 1 receptor agonist; SGLT2: sodium-glucose co-transporter 2; IHD: ischemic heart disease.

Cardiovascular events (n=64)	n
Ischemic heart disease	31
Non-fatal myocardial infarction	11
Coronary revascularization	20
Stroke	19
Hospitalization for heart failure	9
All-cause mortality	13

Supplementary Table 4: Components comprising the cardiovascular event composite endpoint. In the event of a participant experiencing multiple events, the first occurrence decided the follow-up time and categorization of the cardiovascular event composite endpoint.

	Microalbuminuria n=198 HR (95% CI)	p	CKD G3 n=166 HR (95% CI)	p	CVE n=64 HR (95% CI)	p		eGFR slope, ml/min/1.73m^2 Mean yearly change: -1.01 (-1.27, -0.76)	p
Unadjusted									
Non-proliferative (n=231)	1.78 (1.26, 2.53)	0.001	0.77 (0.47, 1.28)	0.319	2.67 (1.52, 4.69)	<0.001		0.29 (-0.35, 0.95)	0.367
Proliferative (n=52)	1.85 (1.00, 3.42)	<0.050	1.74 (0.91, 3.30)	0.093	2.96 (1.17, 7.49)	0.022		-0.24 (-1.46, 0.97)	0.694
Adjusted									
Non-proliferative	1.53 (1.06, 2.22)	0.024	0.69 (0.41, 1.17)	0.173	2.49 (1.33, 4.67)	0.004		0.13 (-0.53, 0.79)	0.702
Proliferative	1.20 (0.63, 2.29)	0.584	1.64 (0.84, 3.19)	0.146	2.65 (0.95, 7.38)	0.063		-0.38 (-1.57, 0.81)	0.528

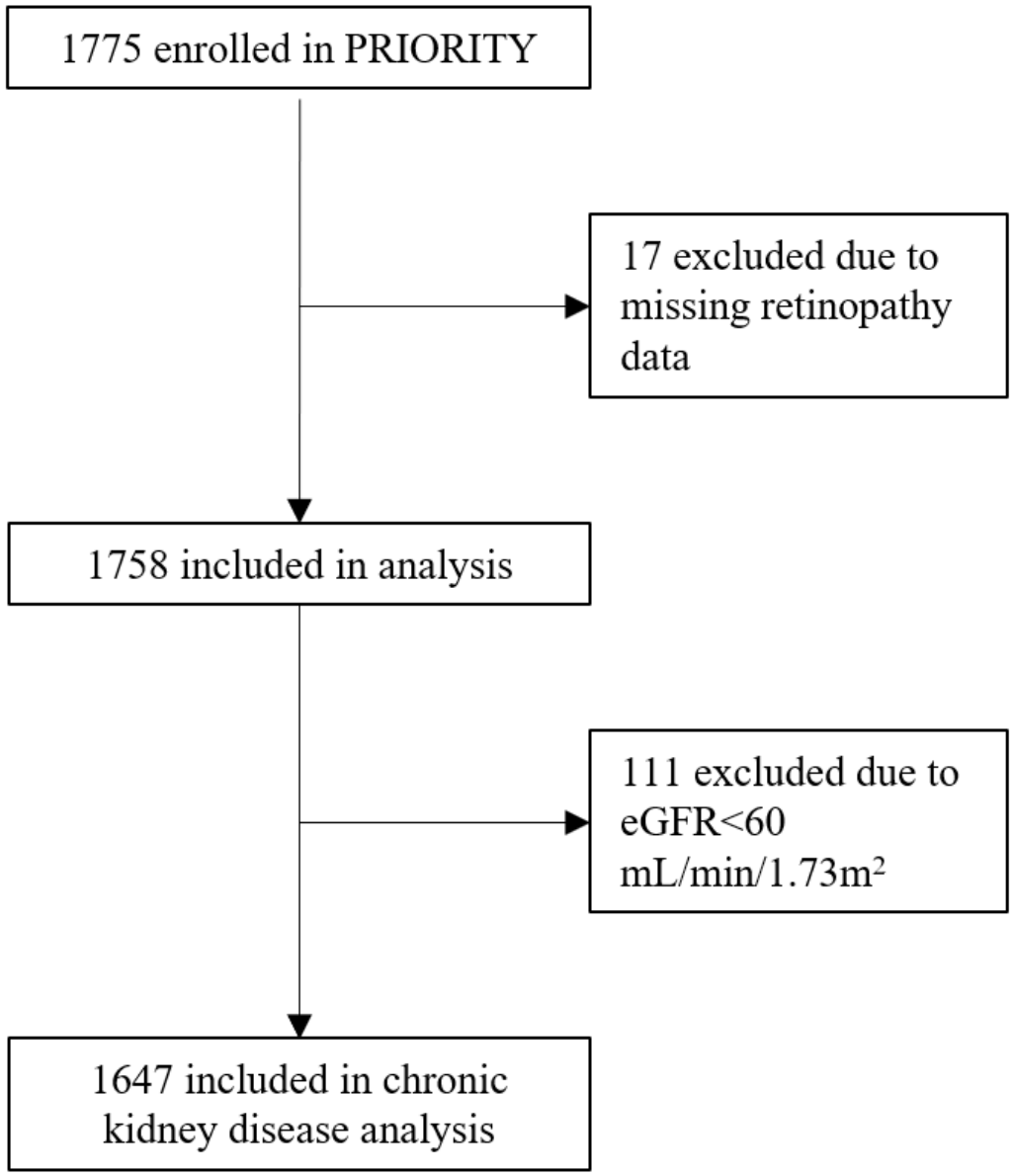
Supplementary Table 5: Unadjusted and adjusted analyses of baseline presence of diabetic retinopathy, stratified by non-proliferative and proliferative DR, in relation to development of dichotomous outcomes (microalbuminuria, chronic kidney disease (CKD), and cardiovascular events (CVE)) and difference in yearly estimated glomerular filtration (eGFR) slope, all compared to no retinopathy. Association to dichotomous outcomes were estimated using Cox proportional hazards models, and association to yearly eGFR slope with linear regression. Adjustment included sex, baseline age, diabetes duration, HbA1c, systolic blood pressure, eGFR, urinary albumin-creatinine rate, and urinary proteomic risk classifier status. Adjustment for the CVE endpoint also included baseline LDL cholesterol, body mass index, and history of ischemic heart disease and stroke.

Outcome	Presence of DR Adjusted HR (95% CI)	p
Microalbuminuria (n=198)	1.46 (1.04-2.06)	0.03
CKD G3 (eGFR<60 mL/min/1.73m^2) (n=166)	0.86 (0.56-1.33)	0.503
CVE (n=64)	2.7 (1.48-4.91)	0.001
	Presence of DR Adjusted mL/min/1.73m^2/year	
eGFR slope difference	-0.03 (-0.63-0.56)	0.912

Supplementary Table 6: Sensitivity analysis of primary results including further adjustment for baseline medication treatments. Presence of diabetic retinopathy (DR) with the development of microalbuminuria, chronic kidney disease (CKD) G3, or cardiovascular events (CVE), and difference in yearly estimated glomerular filtration (eGFR) slope, compared to no diabetic retinopathy. Associations to dichotomous outcomes were estimated using Cox proportional hazards models and association to yearly eGFR slope with linear regression. Adjustments included sex, baseline age, diabetes duration, HbA1c, systolic blood pressure, eGFR, urinary albumin-creatinine rate, urinary proteomic risk classifier status, treatment with renin-angiotensin-aldosterone inhibitor, sodium-glucose cotransporter 2 inhibitor, and glucagon-like peptide 1 receptor agonist. Adjustments for the CVE endpoint also included baseline LDL cholesterol, body mass index, ischemic heart disease and stroke history, treatment with aspirin, and treatment with statins.

	Unadjusted HR (95% CI)	p	Adjusted HR (95% CI)	p
Full cohort n=1758	1.37 (0.55, 3.39)	0.500	1.28 (0.49, 3.30)	0.615
Subset all developing CKD G3 n=166	1.35 (0.54, 3.34)	0.522	1.77 (0.58, 5.42)	0.320
Subset all developing microalbuminuria n=198	0.71 (0.28, 1.76)	0.455	0.79 (0.29, 2.18)	0.650

Supplementary Table 7: Unadjusted and adjusted analyses of baseline presence of diabetic retinopathy in association with a combined endpoint of microalbuminuria and CKD G3 (n=27). This is stratified into populations of the full cohort, a subset of only participants experiencing the CKD G3 event, and finally a subset of only participants experiencing the microalbuminuria event. Adjustment included sex, baseline age, diabetes duration, HbA1c, systolic blood pressure, eGFR, urinary albumin-creatinine rate, and urinary proteomic risk classifier status.



Supplementary Figure 1: Flowchart describing participants included in the present study. eGFR: Estimated glomerular filtration rate.