

Supplemental Materials

Summary of patients included in the analysis

2368 patients randomized

131 deaths by 2 years

109 drop-outs/ non-compliers by 2 years

151 had no baseline creatinine or urine

178 did not have > 2 annual creatinine and urine

81 were randomized in year 2001- 3 (excluded from primary analysis due to missing follow-up creatinine at year 2 and 30)

1799 patients with type 2 diabetes mellitus are included in the analysis.

Supplementary Table 1: Baseline comparison of patients included in renal analysis compared with those who were not included in the analysis.

Characteristic	In renal analysis (N=1799)	Not in renal analysis (N=569)	P Value
Age at study entry, mean, SD	62.0, 8.7	63.5, 9.6	0.0016
Male, %	71.2	67.8	
Race/Ethnicity, %			
Non Hispanic White	66.7	63.3	<0.001
Non Hispanic Black	15.5	21.1	
Hispanic	12.3	13.4	
Asian	5.0	1.6	
Other	0.6	0.7	
BMI, mean, SD	31.6, 5.8	32.3, 6.5	0.0192
COPD, %	3.6	9.6	<0.001
History of MI, %	32.3	31.2	
Sitting systolic BP, mean, SD	131.5, 20.4	132.3, 18.7	
Sitting diastolic BP mean, SD	74.8, 11.3	73.7, 10.9	0.0598
Core: HbA1c %, mean, SD	7.7, 1.6	7.6, 1.6	
Serum creatinine mg/dl, median, IQR	1.0 (0.9 – 1.2)	1.0 (0.8 – 1.2)	0.0519
Urine albumin/creatinine ratio mg/g, median, IQR	11.7, (5.1 – 43.5)	17.9, (6.5 – 78.1)	<0.001
eGFR, mean, SD	76.6, 20.1	73.9, 21.3	0.0175
Duration of DM, median, IQR	8.3, (3.6 – 15.0)	9.5, (4.1 – 16.3)	0.0363
Metformin Use, %	55.6	48.8	0.0043
TZD Use, %	18.4	20.3	
Currently taking insulin, %	25.7	34.9	<0.001
Sulfonylurea, %	55.1	47.9	0.0026

Supplementary Table 2. Yearly Progression of ACR in Patients with Low Normal Albuminuria in IS vs. IP

ACR Category	Baseline N = 818		Year 1 N = 623		Year 2 N=693		Year 3 N = 721		Year 4 N = 608		Year 5 N = 392	
	IS n=421	IP n=397	IS n=367	IP n=256	IS n=369	IP n=324	IS n=366	IP n=355	IS n=304	IP n=304	IS n=192	IP n=200
Low Normal 0-10 mg/g	421 100%	397 100%	252 68.7%	202 78.9%	236 64.0%	237 73.2%	234 63.9%	257 72.4%	189 62.2%	217 71.4%	121 63.0%	134 67.0%
High Normal 10-30 mg/g	--	--	84 22.9%	40 15.6%	98 26.6%	70 21.6%	87 23.8%	70 19.7%	68 22.4%	61 20.1%	45 23.4%	52 26.0%
Micro 30-300 mg/g	--	--	30 8.2%	14 5.5%	33 8.9%	17 5.3%	43 11.8%	27 7.6%	45 14.8%	24 7.9%	26 13.5%	14 7.0%
Macro 300+	--	--	1 0.27%	0 0.0%	2 0.5%	0 0.0%	2 0.6%	1 0.3%	2 0.7%	2 0.7%	0 0.0%	0 0.0%

Supplementary Table 3: Sensitivity analyses based on completeness of data: Number (%) of patients characterized by completeness of data available and ACR progression in IS vs. IP in subgroups based on completeness of data

	N= 1799 with at least 2 follow up visits	IS vs. IP Odds Ratio	95% CI	P Value
Complete (all measures until study end)	996 (55%)	1.37	1.001 – 1.88	0.049
Partially complete (sporadic missing)	747 (41.5%)	1.94	1.31 – 2.88	0.001
Drop-outs (death, inactivation)	56(7.5%)	0.79	0.18 – 3.43	0.75

The *P* Value for the interaction between Randomized treatment and completion status is 0.27.
 Model also includes Cardiac randomization assignment, baseline eGFR, baseline ACR, and year of follow-up

Supplementary Table 4a. ACR progression in IS vs. IP utilizing all available urines collected including those during years 2002, 2003 when serum creatinine was not available on all subjects (N = 1849).

ACR cutoff points	OR	95% CI	P Value
Standard cutoff points	1.25	0.97 – 1.60	0.079
4 category cutoff points	1.38	1.11 – 1.71	0.0043
Gender specific cutoff points	1.51	1.19 – 1.92	<0.001

Odds ratios (OR's) for progression of albuminuria using different cutoff points for micro and macro albuminuria are shown. The standard cutoff point shows the OR for albumin/creatinine ratio (ACR) progression in IS treated patients when ACR progression is defined as a doubling of ACR to at least 100 mg/g, or a change in category (normal to microalbuminuria (≥ 30 mg/g), micro to macroalbuminuria (≥ 300 mg/g)).

The 4 category model includes the additional categories of low normal (<10 mg/g) and high normal (10-29.9 mg/g) albuminuria as well as micro and macroalbuminuria.

The Third row shows the OR for ACR progression using gender specific cutoff points for albuminuria (microalbuminuria 17-250 mg/g for men; 25-355 mg/g for women).

Covariates in this model of ACR progression include cardiac randomization, baseline ACR, baseline EGFR and indicator for follow-up year.

Table 4b. Multivariable Models: Odds ratios for progression of albuminuria in IS compared to IP utilizing all available urines collected including those during years 2002, 2003 when serum creatinine was not available on all subjects (N = 1849).

ACR cutoff points	OR	95% CI	P Value
Standard cutoff points	1.38	1.07 – 1.79	0.013
4 category cutoff points	1.50	1.20 – 1.88	<0.001
Gender specific cutoff points	1.65	1.29 – 2.10	< 0.001

These models are adjusted for cardiac randomization, baseline ACR, baseline EGFR and indicator for follow-up year, race/ethnicity, sex, baseline factors of diabetes duration, BMI, Systolic and diastolic BP, COPD, insulin use, smoking status, triglycerides, HDL, LDL, and concurrent ace/ARB use and HbA1c.