Supplemental Table 1: Comparison of clinical characteristics of patients with T1D in Q1-3 vs. Q4 according to baseline concentrations of circulating TNFR2.

	TNFR2 Q1-Q3 (n=471)	TNFR2 Q4 (n=157)	p value
Patient characteristic			
% Male	51	54	0.44
Age (yrs)	35±11	40±11	<0.0001
Body mass index (kg/m^2)	26±5	26±5	0.22
Systolic blood pressure (mmHg)	121±13	124±15	0.03
Diastolic blood pressure (mmHg)	74±8	73±9	0.51
Serum cholesterol (mg/dl)	193±36	191±36	0.56
Ever smoking (%)	47	47	0.96
Age at diabetes diagnosis (yrs)	16±10	18±10	0.016
Diabetes duration (yrs)	19±9	22±9	<0.0001
HbA1c (%)	8.6±1.6	8.6±1.5	0.48
AER (µg/min)	43 (26, 81)	51 (30, 124)	0.028
eGFRcystatin (ml/min/1.73m^2)	138±27	110±28	<0.0001
Treated with RASi/AHTN (%)	41	57	0.003
Historical cohort (%)	44	42	0.72

Data are mean±SD; median (25th, 75th percentiles) or percents. Body mass index is the weight in kilograms divided by the square of the height in meters.

Abbreviations: TNFR2 - TNF receptor type 2, Q1-Q3 (quartile 1 to 3), Q4 – quartile 4, T1D denotes type 1 diabetes, AER - albumin excretion rate, eGFRcystatin - glomerular filtration rate estimated by serum cystatin C, HbA1c - hemoglobin A1c, RASi/AHTN - renin-angiotensin system inhibitors and/or other antihypertensive agent, TNFR2 - TNF receptor type 2.

Supplemental Table 2: Incidence rate of CKD≥3 in the 2nd Joslin Kidney Study patients with T1D during 5-12 year follow-up according to quartiles of the distributions of baseline circulating concentrations of the TNF receptors 1 and 2 in serum and urine.

		TNFR1		**TNFR2**	
Quartile*		**serum**	**urine**	**serum**	**urine**
Number of patients		Incidence rate†	Incidence rate†	Incidence rate†	Incidence rate†
Q1	88	2 (1)	13 (6)	7 (3)	11 (5)
Q2	89	5 (2)	13 (6)	0 (0)	16 (7)
Q3	88	6 (3)	11 (5)	10 (5)	11 (5)
Q4	88	59 (25)	30 (13)	55 (23)	30 (13)
P for trend[‡]		*P<0.001*	*P=0.22*	*P<0.001*	*P=0.18*

* Quartile boundaries:	25th percentile	50th percentile	75th percentile
serum TNFR1 (pg/ml):	1180	1380	1710
urine TNFR1 (ng/g cr):	875	1378	1940
serum TNFR2 (pg/ml):	1869	2230	2695
urine TNFR2 (ng/g cr):	985	1627	2350

† per 1000 person years, ( ) number of events.

‡ Bonferroni correction was applied.

Abbreviations: CKD denotes chronic kidney disease stage, T1D - type 1 diabetes, TNFα - tumor necrosis factor alpha; TNFR1 - TNF receptor type 1; TNFR2 - TNF receptor type 2, Q1-Q4 - quartile 1 to 4.

Supplemental Table 3: Cox proportional hazard analysis of the risk of CKD≥3 in the 2nd Joslin Kidney Study patients with T1D according to TNFR1 and TNFR2 in serum and urine.

	Crude model HR [95% C.I.]	Adjusted model HR [95% C.I.]
TNFR: Q4 vs. Q1-3		
TNFR1		
serum	13.4 [5.5, 32.8]	12.9 [5.3, 31.7] [†]
urine*	2.4 [1.2, 5.0]	2.1 [1.0, 4.3] [†§]
TNFR2		
serum	9.2 [4.1, 20.7]	8.5 [3.7, 19.7] [‡]
urine*	2.3 [1.1, 4.7]	1.3 [0.6, 2.7] [‡§]

* Quartiles of the urinary markers were based on the concentrations of TNFR1 or TNFR2 normalized to creatinine.

† Effects of both serum and urinary TNFR1 concentrations are considered in the model.

‡ Effects of both serum and urinary TNFR2 concentrations are considered in the model.

§ Hazard ratios for urinary concentrations of TNFR1, and TNFR2 have no longer been significant in the respective adjusted model.

Abbreviations: T1D denotes type 1 diabetes, CKD – chronic kidney disease stage, HR – hazard ratios, CI – confidence intervals, TNFR1 - TNF receptor 1, TNFR2 - TNF receptor 2, Q1-Q4 - quartile 1 to 4.

Supplemental Table 4: Risk of regression and progression of AER during 5-7 years of follow-up according to baseline quartiles of TNFR1, TNFR2, in the 2nd Joslin Kidney Study.

Marker	Quartile† range	Number of patients	Regression of AER * (percent)	Progression of AER* (percent)
TNFR1				
	Q1	88	36	19
	Q2	88	45	16
	Q3	89	29	21
	Q4	88	33	31
	Test of trend		p=ns	p=0.05 (ns after Bonferroni correction)
TNFR2				
	Q1	89	38	12
	Q2	88	39	20
	Q3	88	39	20
	Q4	88	30	34
	Test of trend		p=ns	p=0.01 (nominally significant after Bonferroni correction)

* Definition of regression and progression of AER, please see our previous publication
(Ficociello et al. Diabetes Care 2010: 33:1337-1343)

† Quartile boundaries:	25th percentile	50th percentile	75th percentile
TNFR1 (pg/ml):	1180	1380	1710
TNFR2 (pg/ml):	1869	2230	2695

Abbreviations: AER – albumin excretion rate, JKS – Joslin Kidney Study. TNFR1 - TNF receptor 1, TNFR2 - TNF receptor 2, Q1-Q4

- quartile 1 to 4.