SUPPLEMENTARY DATA

Effect of Saxagliptin on Renal Outcomes in the SAVOR TIMI-53 study- Appendixes:

Supplementary Appendix Table 1. Number and % of patients at the saxagliptin and placebo arms, according to eGFR and on treatment ACR groups at baseline, 1 year, and EOT

n (% from ACR by treatment arm)	**eGFR>50 ml/min/BSA**					
	ACR<30 Mg/G		**30≤ACR≤300 Mg/G**		**ACR>300 Mg/G**	
	saxagliptin	**placebo**	**saxagliptin**	**placebo**	**saxagliptin**	**placebo**
baseline	4365 (65.3%)	4326 (65.2%)	1805 (27.0%)	1819 (27.4%)	513 (7.7%)	491 (7.4%)
1 year	3847 (68.7%)	3566 (65.3%)	1333 (23.8%)	1454 (26.6%)	418 (7.5%)	442 (8.1%)
EOT	3311 (65.8%)	3063 (62.9%)	1328 (26.4%)	1379 (28.3%)	390 (7.8%)	427 (8.8%)

n (% from ACR by treatment arm)	**30≤eGFR≤50 ml/min/BSA**					
	ACR<30 Mg/G		**30≤ACR≤300 Mg/G**		**ACR>300 Mg/G**	
	saxagliptin	**placebo**	**saxagliptin**	**placebo**	**saxagliptin**	**placebo**
baseline	470 (44.0%)	474 (44.8%)	362 (33.9%)	346 (32.7%)	237 (22.2%)	239 (22.6%)
1 year	357 (42.9%)	369 (46.2%)	313 (37.6%)	253 (31.7%)	162 (19.5%)	177 (22.2%)
EOT	295 (41.7%)	279 (41.0%)	265 (37.5%)	230 (33.8%)	147 (20.8%)	172 (25.3%)

n (% from ACR by treatment arm)	**eGFR<30 ml/min/BSA**					
	ACR<30 Mg/G		**30≤ACR≤300 Mg/G**		**ACR>300 Mg/G**	
	saxagliptin	**placebo**	**saxagliptin**	**placebo**	**saxagliptin**	**placebo**
baseline	32 (19.5%)	29 (19.5%)	50 (30.5%)	44 (29.5%)	82 (50.0%)	76 (51.0%)
1 year	23 (19.2%)	26 (23.2%)	47 (39.2%)	28 (25.0%)	50 (41.7%)	58 (51.8%)
EOT	20 (19.6%)	18 (20.5%)	39 (38.2%)	27 (30.7%)	43 (42.2%)	43 (48.9%)

(Abbreviations: BSA Body Surface area **per 1.73 m^2**)

SUPPLEMENTARY DATA

Supplementary Appendix Table 2. Multivariable Analysis of the association between baseline variables and ACR and eGFR as continuous variable at baseline

	Multivariable Modeling for log(ACR) (mg/g) at baseline			Multivariable Modeling for eGFR (mL/min/BSA) at baseline		
Variable*	**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Age (increase by a year)	0.0015	(-0.0019, 0.0050)	0.3855	-0.7425	(-0.7838, -0.7011)	<.0001
Sex (Male vs. Female)		NS		5.0366	(4.3397, 5.7334)	<.0001
Race (Caucasian vs. all other)	-0.3712	(-0.4348, -0.3076)	<.0001	-0.7842	(-1.5914, 0.0230)	0.0569
Hispanic or Latino (vs. not)	0.3113	(0.2456, 0.3770)	<.0001	3.0296	(2.2090, 3.8501)	<.0001
BMI (kg/m2)		NS		-0.2121	(-0.2735, -0.1506)	<.0001
Duration of diabetes (for each extra year)	0.0184	(0.0151, 0.0218)	<.0001	-0.1087	(-0.1497, -0.0677)	<.0001
Current smoker		NS		3.1464	(2.1880, 4.1049)	<.0001
History of CVD	0.2050	(0.1411, 0.2689)	<.0001	-1.4584	(-2.2857, -0.6311)	0.0005
HbA1C% (unit increase in HbA1c)	0.1857	(0.1618, 0.2097)	<.0001	0.4320	(0.1374, 0.7266)	0.0041
Fasting PG (mg/dl for each unit increase)	0.0010	(0.0005, 0.0016)	0.0003	0.0179	(0.0109, 0.0248)	<.0001
eGFR (ml/min/BSA)	-0.0151	(-0.0164, -0.0138)	<.0001			
ACR (analyzed on a log scale for each percentage point increase for the ACR, the GFR decreases by 2.7)		NA		-2.3757	(-2.5662, -2.1851)	<.0001
ACE inhibitors	0.0780	(0.0157, 0.1403)	0.0141		NS	
ARBs	0.2455	(0.1764, 0.3146)	<.0001	-1.8087	(-2.5251, -1.0924)	<.0001
B-Blockers		NS		-2.9851	(-3.6860, -2.2841)	<.0001
Statin		NS		-1.0403	(-1.8543, -0.2264)	0.0122
Aspirin		NS			NS	
Sulfonylurea	-0.0303	(-0.0881, 0.0276)	0.3055	-0.9703	(-1.6753, -0.2654)	0.0070
Metformin	-0.0340	(-0.0943, 0.0262)	0.2687	7.8730	(7.1487, 8.5973)	<.0001
Insulin	0.2701	(0.2045, 0.3356)	<.0001	-1.6524	(-2.4561, -0.8488)	<.0001
Thiazolidinediones	-0.0571	(-0.1682, 0.054)	0.3138		NS	

(Abbreviations: BSA Body Surface area **per 1.73 m^2**)

SUPPLEMENTARY DATA

Supplementary Appendix Table 3. Change in categorical ACR (<15mg/g, >=15 and<30 mg/g, 30-<100 mg/g, 100-300 mg/g, >300 mg/g) from baseline to EOT by baseline ACR categories and treatment arms

		ACR (Mg/G) at EOT									
		SAXAGLIPTIN					PLACEBO				
		<15	≥15-<30	≥30-<100	≥100-≤300	>300	<15	≥15-<30	≥30-<100	≥100-≤300	>300
ACR (Mg/G) at baseline	<15 P*= 0.019	2204 75.5%	410 14.0%	246 8.4%	43 1.5%	17 0.6%	2056 72.8%	447 15.8%	247 8.7%	60 2.1%	15 0.5%
	≥15-<30 P**= 0.090	323 39.2%	215 26.1%	219 26.6%	47 5.7%	19 2.3%	273 33.5%	217 26.6%	260 31.9%	50 6.1%	16 2.0%
	≥30-<100 P**<0.001	193 18.5%	181 17.4%	434 41.6%	184 17.6%	51 4.9%	144 14.5%	159 16.1%	395 39.9%	205 20.7%	87 8.8%
	≥100-≤300 P**=0.043	38 7.3%	39 7.5%	137 26.4%	174 33.6%	130 25.1%	25 4.9%	24 4.7%	136 26.4%	168 32.6%	162 31.5%
	>300 P***=0.049	13 2.4%	10 1.9%	45 8.4%	103 19.3%	363 68.0%	9 1.8%	6 1.2%	28 5.7%	87 17.7%	362 73.6%

*P-value is based on a two tailed normal distribution approximation test for the proportion of patients who worsened

** P-value is based on a chi-squared test for independence

***P-value is based on a two tailed normal distribution approximation test for the proportion of patients who improved

P-values were calculated for each level of ACR at baseline separately.

White: The number of patients (%) at each ACR category at baseline, with no change in ACR category to EOT.

Very Light Green: The number of patients (%) at each ACR category at baseline, with improvement in one ACR category to EOT.

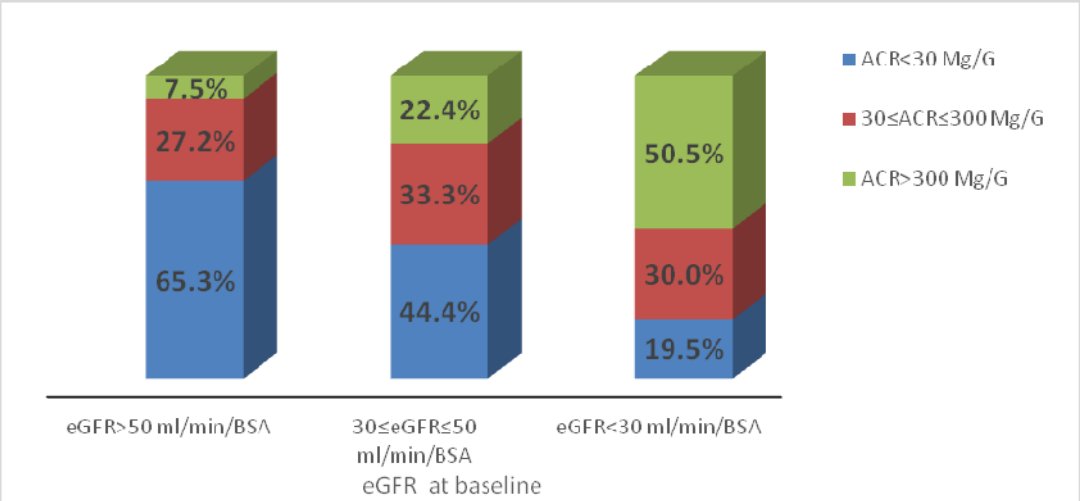
Light Green: The number of patients (%) at each ACR category at baseline, with improvement in two ACR categories to EOT.

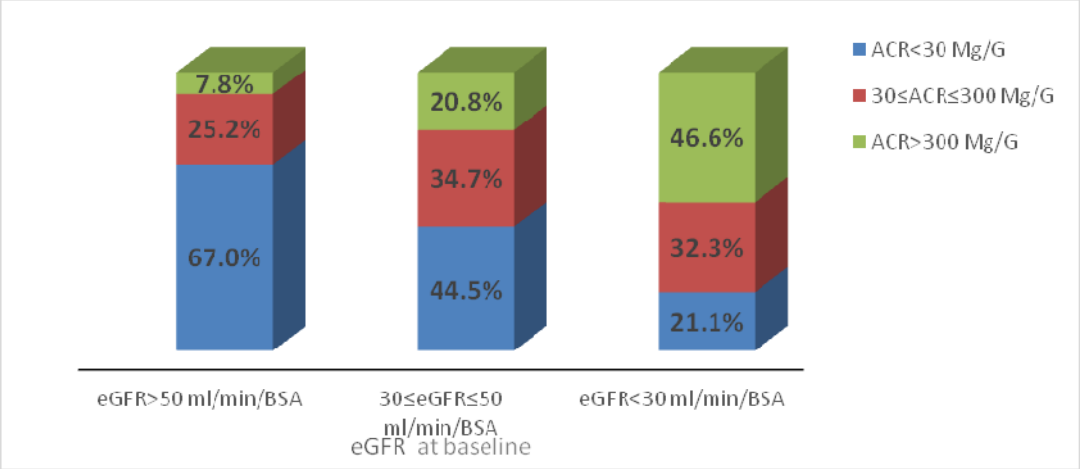
Moderate Green: The number of patients (%) at each ACR category at baseline, with improvement in three ACR categories to EOT.

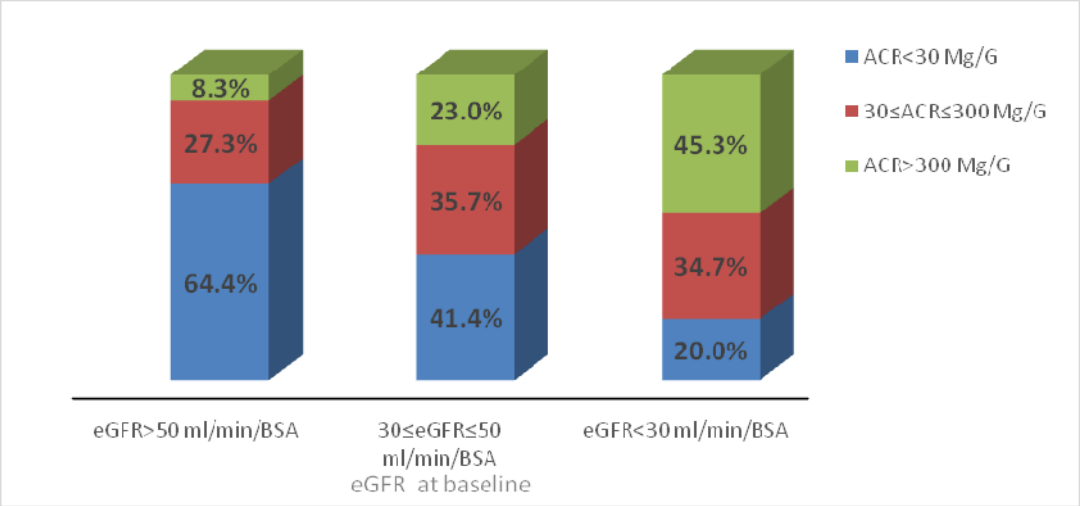
Dark Green: The number of patients (%) at each ACR category at baseline, with improvement in four ACR categories to EOT.

SUPPLEMENTARY DATA

Supplementary Appendix Figure 1. Percentage of patients at the different on treatment ACR (at Baseline, 1year and EOT) categories out of the patients at baseline eGFR category



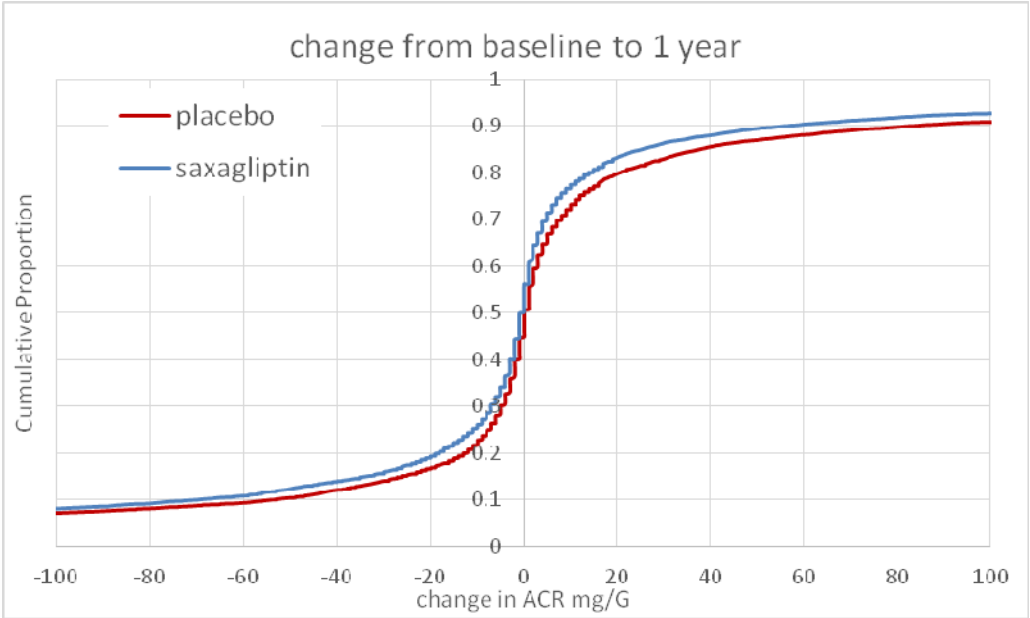




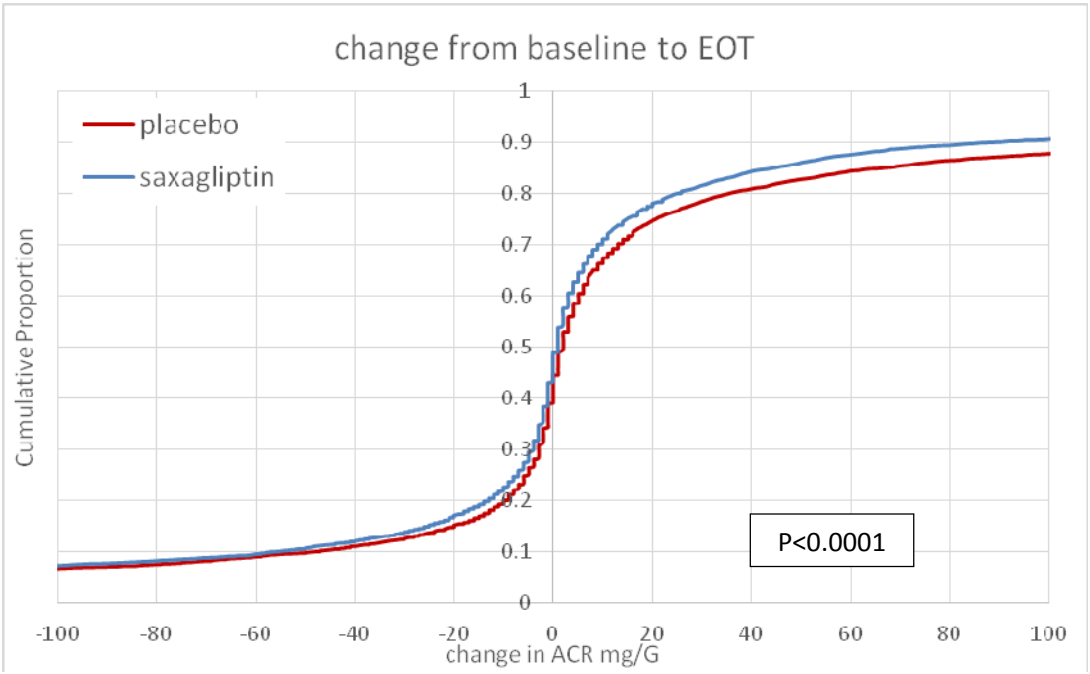
SUPPLEMENTARY DATA

Supplementary Appendix Figure 2. Density charts for change of ACR from baseline to 1 year and EOT, by treatment arms*

A- 1 year



B- EOT



(For visualization purposes the graph was drawn with change in ACR values cut-off between -100 and 100)