

SUPPLEMENTARY DATA

Supplementary Table S1. Hematocrit (%) by time point through 52 weeks of treatment

	Placebo	SOTA 200 mg	SOTA 400 mg
	(n = 526)	(n = 524)	(n = 525)
Baseline			
N	523	523	524
Mean (SE)	41.96 (0.16)	41.85 (0.16)	41.98 (0.16)
Week 12			
N	497	497	504
LS mean CFB (SE)	0.12 (0.11)	1.88 (0.11)	2.00 (0.11)
LS mean difference (SE) vs. placebo		1.76 (0.15)	1.88 (0.15)
95% CI		1.46 , 2.05	1.59 , 2.17
P-value		<0.0001	<0.0001
Week 24			
N	483	484	487
LS mean CFB (SE)	0.13 (0.12)	1.78 (0.12)	1.97 (0.12)
LS mean difference (SE) vs. placebo		1.65 (0.16)	1.84 (0.16)
95% CI		1.34 , 1.96	1.53 , 2.15
P-value		<0.0001	<0.0001
Week 52			
N	378	390	377
LS mean CFB (SE)	0.02 (0.13)	1.83 (0.13)	1.92 (0.13)
LS mean difference (SE) vs. placebo		1.81 (0.17)	1.89 (0.17)
95% CI		1.48 , 2.14	1.56 , 2.23
P-value		<0.0001	<0.0001

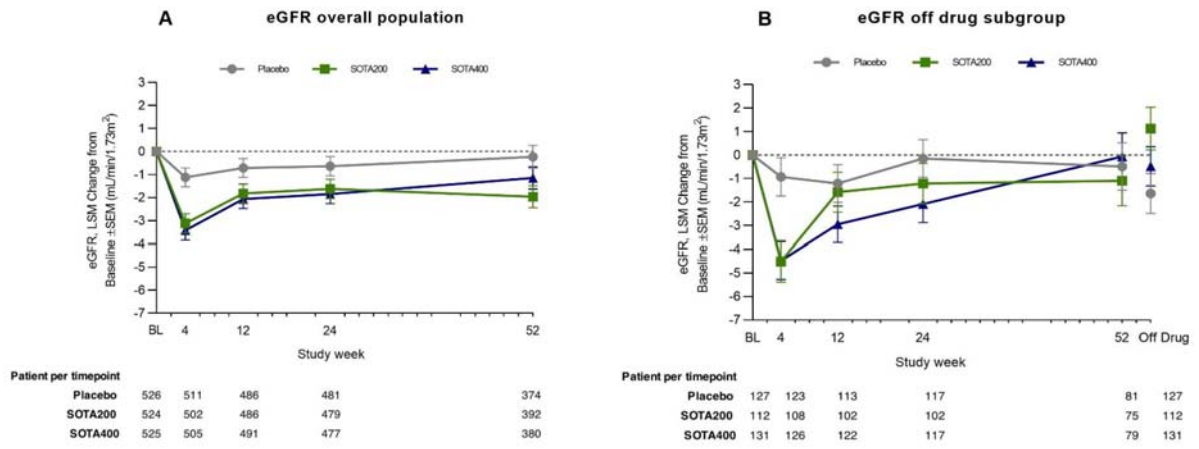
SUPPLEMENTARY DATA

Supplementary Table S2. Uric acid (mg/dL) by time point through 52 weeks of treatment

	Placebo	SOTA 200 mg	SOTA 400 mg
	(n = 526)	(n = 524)	(n = 525)
Baseline			
N	526	524	525
Mean (SE)	4.51 (0.05)	4.53 (0.05)	4.45 (0.05)
Week 4			
N	512	502	505
LS mean CFB (SE)	0.04 (0.03)	-0.25 (0.03)	-0.38 (0.03)
LS mean difference (SE) vs. placebo		-0.29 (0.04)	-0.42 (0.04)
95% CI		-0.37, -0.21	-0.50, -0.34
P-value		<0.0001	<0.0001
Week 12			
N	487	486	492
LS mean CFB (SE)	0.03 (0.03)	-0.22 (0.03)	-0.29 (0.03)
LS mean difference (SE) vs. placebo		-0.25 (0.04)	-0.32 (0.04)
95% CI		-0.33, -0.16	-0.40, -0.23
P-value		<0.0001	<0.0001
Week 24			
N	479	478	477
LS mean CFB (SE)	0.05 (0.03)	-0.21 (0.03)	-0.29 (0.03)
LS mean difference (SE) vs. placebo		-0.26 (0.05)	-0.33 (0.05)
95% CI		-0.35, -0.17	-0.42, -0.24
P-value		<0.0001	<0.0001
Week 52			
N	374	393	381
LS mean CFB (SE)	-0.07 (0.04)	-0.24 (0.04)	-0.35 (0.04)
LS mean difference (SE) vs. placebo		-0.17 (0.05)	-0.28 (0.05)
95% CI		-0.27, -0.08	-0.37, -0.18
P-value		0.0003	<0.0001

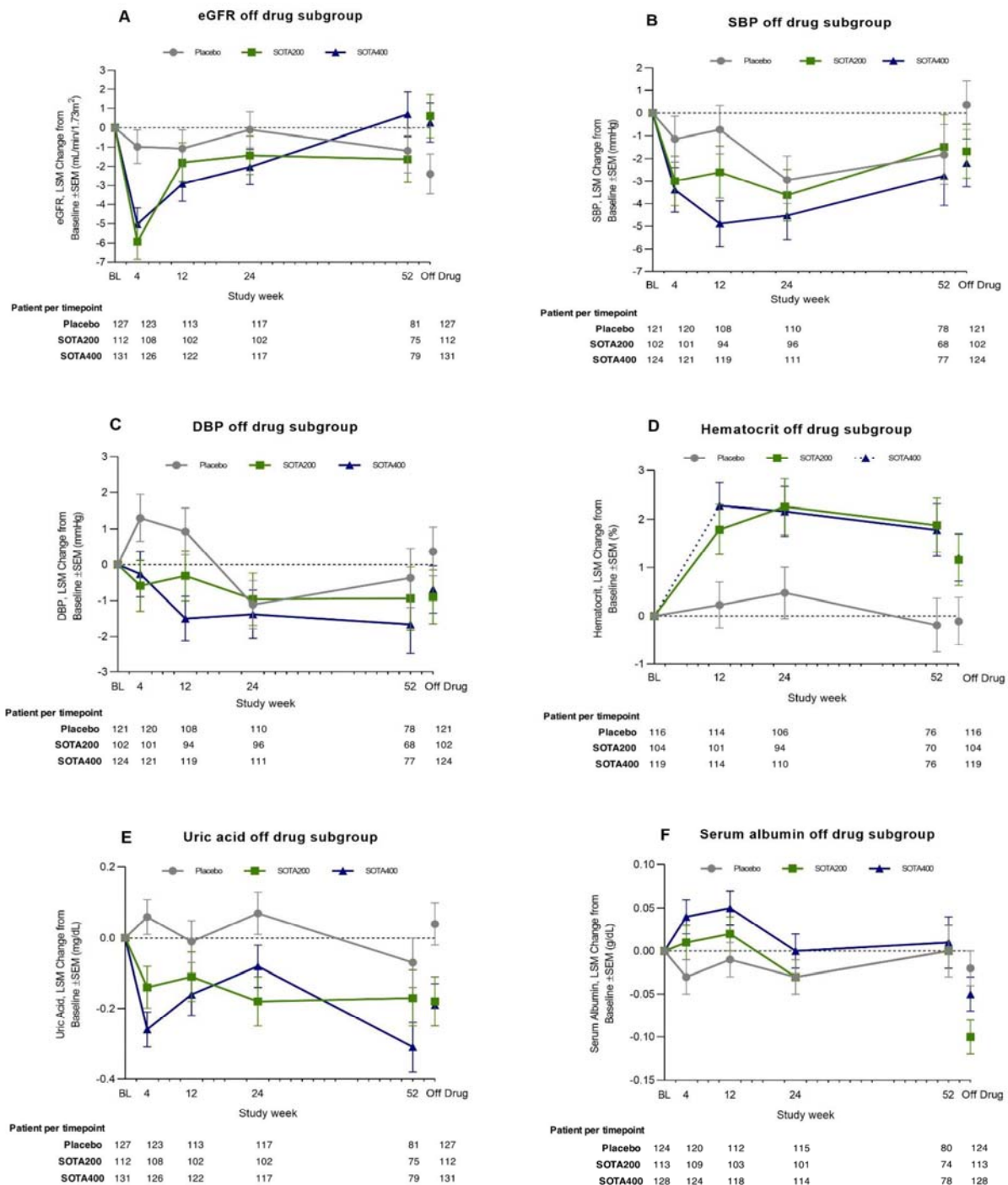
SUPPLEMENTARY DATA

Supplementary Figure S1. eGFR CKD-EPI



SUPPLEMENTARY DATA

Supplementary Figure S2. “Off drug” subgroup analysis 7 days after the last dose of SOTA



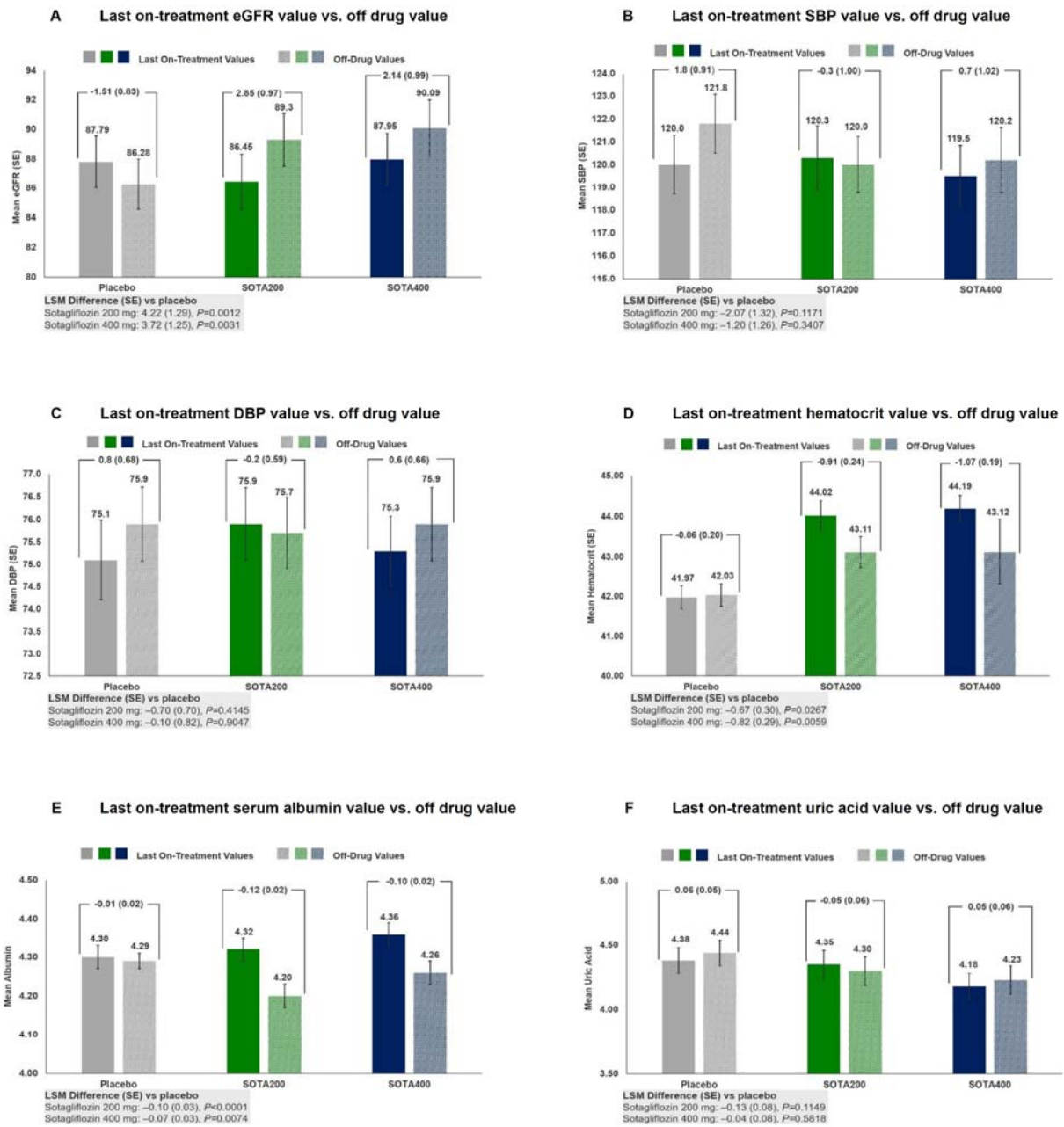
Subgroup of patients with off drug record. Off drug is defined as 7 days after last dose, with the window of 5–28 days. (A) eGFR. LS mean change (95% CI) from baseline vs. placebo at Week 52 for SOTA 200 mg: $-0.4 \text{ mL/min/1.73 m}^2$ ($-3.60, 2.73$), $P = 0.79$; SOTA 400 mg: $1.9 \text{ mL/min/1.73 m}^2$ ($-1.23, 5.00$), $P = 0.23$; Change from baseline with off drug record vs. placebo (95% CI) for SOTA 200 mg: 3.0

SUPPLEMENTARY DATA

mL/min/1.73 m² (0.27, 5.70), $P = 0.031$; SOTA 400 mg: 2.7 mL/min/1.73 m² (0.06, 5.27), $P = 0.045$. (B) SBP. LS mean change (95% CI) from baseline vs. placebo at Week 52 for SOTA 200 mg: 0.3 mmHg (-3.34 to 4.01), $P = 0.86$, SOTA 400 mg -0.9 mmHg (-4.48 to 2.61), $P = 0.60$; Change from baseline with off drug record vs. placebo (95% CI) for SOTA 200 mg: -2.0 mmHg (-4.89 to 0.83), $P = 0.16$; SOTA 400 mg: -2.5 mmHg (-5.26 to 0.17), $P = 0.066$. (C) DBP. LS mean change (95% CI) from baseline vs. placebo at Week 52 for SOTA 200 mg: -0.6 mmHg (-2.86 to 1.74), $P = 0.63$, SOTA 400 mg -1.3 mmHg (-3.51 to 0.94), $P = 0.26$; Change from baseline with off drug record vs. placebo (95% CI) for SOTA 200 mg: -1.3 mmHg (-3.08 to 0.53), $P = 0.17$; SOTA 400 mg: -1.1 mmHg (-2.77 to 0.65), $P = 0.22$ (D) Hematocrit. LS mean change (95% CI) from baseline vs. placebo at Week 52 for SOTA 200 mg: 2.1% (1.35 to 2.81), $P < 0.0001$, SOTA 400 mg -2.0% (1.26 to 2.69), $P < 0.0001$; Change from baseline with off drug record vs. placebo (95% CI) for SOTA 200 mg: 1.3% (0.62 to 1.93), $P < 0.0001$; SOTA 400 mg: 1.3% (0.69 to 1.95), $P < 0.0001$ (E) Serum uric acid. LS mean change (95% CI) from baseline vs. placebo at Week 52 for SOTA 200 mg: -0.1 mg/dL (-0.30 to 0.10), $P = 0.33$, SOTA 400 mg -0.2 mg/dL (-0.43 to -0.05), $P = 0.016$; Change from baseline with off drug record vs. placebo (95% CI) for SOTA 200 mg: -0.2 mg/dL (-0.39 to -0.05), $P = 0.0096$; SOTA 400 mg: -0.2 mg/dL (-0.40 to -0.08), $P = 0.0040$ (F) Serum albumin. LS mean change (95% CI) from baseline vs. placebo at Week 52 for SOTA 200 mg: -0.00 g/dL (-0.07 to 0.07), $P = 0.97$, SOTA 400 mg: 0.01 g/dL (-0.06 to 0.08), $P = 0.85$; Change from baseline with off drug record vs. placebo (95% CI) for SOTA 200 mg: -0.08 g/dL (-0.13 to -0.02), $P = 0.0078$; SOTA 400 mg: -0.02 g/dL (-0.08 to 0.03), $P = 0.44$.

SUPPLEMENTARY DATA

Supplementary Figure S3.



The last on-treatment value for a laboratory and vital signs variable is defined as the last value collected or taken, from both scheduled and unscheduled assessments, after the first dose of study drug and no more than 1 day after the last dose of study drug.