Supplemental Material

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Supplementary Table 1. Distribution of randomized patients by 33 study sites (*N*=130).

Site No.	TMX-049 200 mg (*n*=44)	TMX-049 40 mg (*n*=44)	Placebo (*n*=42)
002	0	0	1
003	2	1	0
004	1	0	0
005	2	1	0
006	1	1	0
007	1	1	2
008	0	2	0
009	1	1	1
010	2	4	1
011	0	2	0
013	0	2	2
014	3	0	3
015	0	2	1
016	6	7	7
018	4	2	0
019	0	0	1
020	0	1	0
021	0	0	1
024	0	1	1
026	8	5	7
027	0	0	1
028	1	0	1
029	0	2	1
031	2	2	1
032	3	2	2
033	0	0	2
034	1	1	2
039	1	2	1
040	0	0	1
045	1	2	1
046	2	0	1
047	1	0	0
049	1	0	0

Supplementary Table 2. Change in log-transformed UACR from baseline to Week 12 with analyses using an ANCOVA (LOCF), ANCOVA (OC), and MMRM.

Data are presented for the modified intention-to-treat population (*N*=129): TMX-049 200 mg (*n*=44), TMX-049 40 mg (*n*=43), and placebo (*n*=42).

		Log-transformed UACR (mg/g), Mean±standard error (*n*)		Change in log-transformed UACR (mg/g) from baseline to Week 12, LS mean (95% CI)	vs Placebo	
		Baseline	Week 12		The relative ratio of adjusted geometric means of Week 12 to baseline ratio, LS mean (95% CI)	*P* value
ANCOVA [a] (LOCF)	TMX-049 200 mg QD	6.25±0.14 (44)	5.75±0.21 (44)	-0.53 (-0.83, -0.23)	0.65 (0.44, 0.96)	0.0311
	TMX-049 40 mg QD	6.02±0.19 (43)	5.91±0.17 (43)	-0.15 (-0.45, 0.15)	0.95 (0.64, 1.41)	0.7953
	Placebo	6.28±0.15 (42)	6.20±0.18 (42)	-0.10 (-0.40, 0.21)		
ANCOVA [a] (OC)	TMX-049 200 mg QD	6.22±0.14 (43)	5.71±0.20 (43)	-0.54 (-0.84, -0.23)	0.64 (0.43, 0.95)	0.0285
	TMX-049 40 mg QD	5.99±0.19 (42)	5.89±0.18 (42)	-0.14 (-0.44, 0.17)	0.95 (0.64, 1.43)	0.8155
	Placebo	6.26±0.15 (40)	6.19±0.19 (40)	-0.09 (-0.40, 0.22)		
MMRM [b]	TMX-049 200 mg QD	6.25±0.14 (44)	5.71±0.20 (43)	-0.52 (-0.81, -0.23)	0.65 (0.44, 0.97)	0.0341
	TMX-049 40 mg QD	6.02±0.19 (43)	5.89±0.18 (42)	-0.13 (-0.43, 0.16)	0.96 (0.64, 1.43)	0.8364
	Placebo	6.28±0.15 (42)	6.19±0.19 (40)	-0.09 (-0.39, 0.21)		

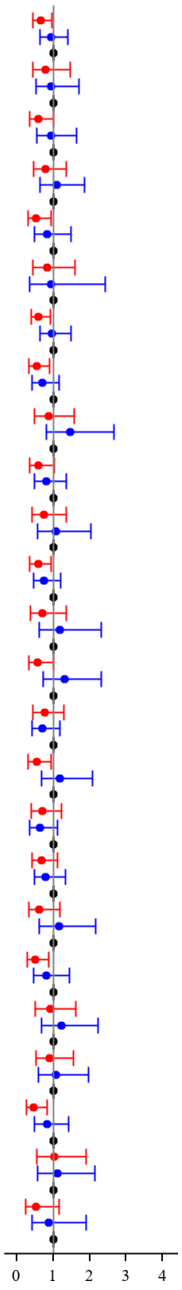
a) ANCOVA, with randomized treatment and randomization strata of the UACR and sUA as independent variables.

b) MMRM, which included randomized treatment, randomization strata of the UACR and sUA, timepoint (week), and a treatment-by-timepoint interaction as fixed effects and patient as a random effect. The restricted maximum likelihood method for estimation was used. Within-patient errors were modeled using an unstructured (co)variance structure. The Kenward-Roger approximation was used to approximate the denominator degrees of freedom.

ANCOVA, analysis of covariance; CI, confidence Interval; LOCF, last-observation carried-forward; LS mean, least squares mean; MMRM, mixed model for repeated measures; OC, observed case; QD, once daily; sUA, serum uric acid; UACR, urine albumin-to-creatinine ratio.

Supplementary Figure 1. Results of a subgroup analysis according to the baseline characteristics: The relative ratio (95% CI) of adjusted geometric means of Week 12 to baseline ratio in UACR between TMX-049 200 mg/40 mg group and placebo group for subgroups.

Data are presented for the modified intention-to-treat population (*N*=129): TMX-049 200 mg (*n*=44), TMX-049 40 mg (*n*=43), and placebo (*n*=42).

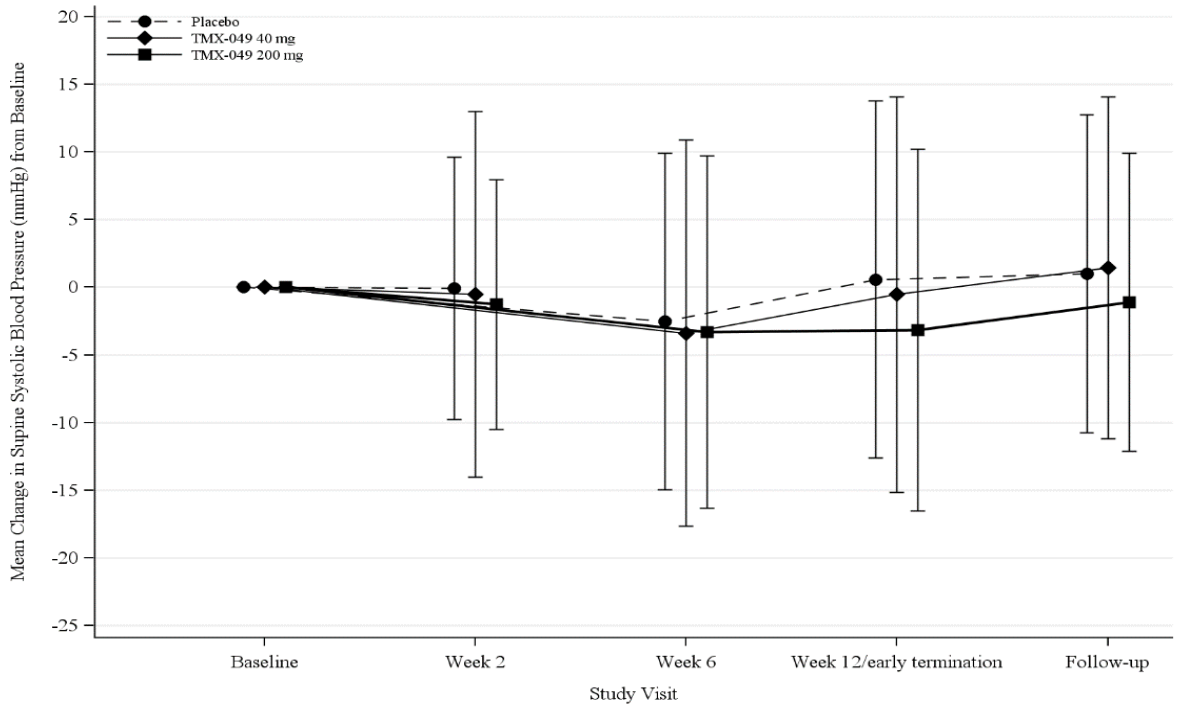


Subgroup	Treatment Group	N	Adjusted Relative Ratio (95%CI)	P Value for interaction
Total population	TMX-049 200 mg	44	0.65 (0.44, 0.96)	
	TMX-049 40 mg	43	0.95 (0.64, 1.41)	
	Placebo	42	-	
< 65 years	TMX-049 200 mg	14	0.80 (0.43, 1.46)	0.717
	TMX-049 40 mg	16	0.95 (0.52, 1.71)	
	Placebo	17	-	
>= 65 years	TMX-049 200 mg	30	0.59 (0.35, 1.01)	
	TMX-049 40 mg	27	0.95 (0.55, 1.64)	
	Placebo	25	-	
Male	TMX-049 200 mg	26	0.79 (0.46, 1.36)	0.563
	TMX-049 40 mg	26	1.09 (0.64, 1.87)	
	Placebo	24	-	
Female	TMX-049 200 mg	18	0.53 (0.30, 0.93)	
	TMX-049 40 mg	17	0.84 (0.47, 1.48)	
	Placebo	18	-	
African-Amerian	TMX-049 200 mg	8	0.83 (0.43, 1.59)	0.758
	TMX-049 40 mg	2	0.93 (0.36, 2.42)	
	Placebo	5	-	
Not Afrian-American	TMX-049 200 mg	36	0.60 (0.39, 0.93)	
	TMX-049 40 mg	41	0.97 (0.63, 1.49)	
	Placebo	37	-	
Baseline eGFR < 60 mL/min/1.73m2	TMX-049 200 mg	26	0.54 (0.32, 0.89)	0.175
	TMX-049 40 mg	24	0.69 (0.41, 1.16)	
	Placebo	24	-	
Baseline eGFR >= 60 mL/min/1.73m2	TMX-049 200 mg	18	0.86 (0.47, 1.58)	
	TMX-049 40 mg	19	1.46 (0.80, 2.66)	
	Placebo	18	-	
BMI < 31.7 kg/m2	TMX-049 200 mg	17	0.59 (0.34, 1.03)	0.775
	TMX-049 40 mg	21	0.81 (0.48, 1.36)	
	Placebo	26	-	
BMI >= 31.7 kg/m2	TMX-049 200 mg	27	0.74 (0.41, 1.35)	
	TMX-049 40 mg	22	1.08 (0.58, 2.03)	
	Placebo	16	-	
SBP < 139 mmHg	TMX-049 200 mg	19	0.58 (0.35, 0.95)	0.537
	TMX-049 40 mg	21	0.75 (0.46, 1.21)	
	Placebo	23	-	
SBP >= 139 mmHg	TMX-049 200 mg	25	0.71 (0.37, 1.36)	
	TMX-049 40 mg	22	1.19 (0.61, 2.31)	
	Placebo	19	-	
sUA < 6.1 mg/dL	TMX-049 200 mg	22	0.57 (0.32, 1.01)	0.058
	TMX-049 40 mg	21	1.30 (0.73, 2.32)	
	Placebo	20	-	
sUA >= 6.1 mg/dL	TMX-049 200 mg	22	0.76 (0.45, 1.28)	
	TMX-049 40 mg	22	0.70 (0.41, 1.19)	
	Placebo	22	-	
UACR < 474 mg/g	TMX-049 200 mg	21	0.54 (0.31, 0.94)	0.067
	TMX-049 40 mg	23	1.18 (0.67, 2.07)	
	Placebo	20	-	
UACR >= 474 mg/g	TMX-049 200 mg	23	0.70 (0.40, 1.22)	
	TMX-049 40 mg	20	0.63 (0.36, 1.12)	
	Placebo	22	-	
HbA1c < 7.6%	TMX-049 200 mg	25	0.68 (0.42, 1.13)	0.444
	TMX-049 40 mg	22	0.80 (0.48, 1.32)	
	Placebo	17	-	
HbA1c >= 7.6%	TMX-049 200 mg	19	0.62 (0.32, 1.18)	
	TMX-049 40 mg	21	1.16 (0.62, 2.16)	
	Placebo	25	-	
hsCRP < 0.312 mg/dL	TMX-049 200 mg	19	0.49 (0.28, 0.88)	0.339
	TMX-049 40 mg	20	0.82 (0.46, 1.43)	
	Placebo	25	-	
hsCRP >= 0.312 mg/dL	TMX-049 200 mg	24	0.91 (0.51, 1.63)	
	TMX-049 40 mg	23	1.23 (0.68, 2.23)	
	Placebo	17	-	
sTNFR1 < 2343.7 ng/L	TMX-049 200 mg	25	0.89 (0.52, 1.55)	0.247
	TMX-049 40 mg	18	1.07 (0.58, 1.96)	
	Placebo	21	-	
sTNFR1 >= 2343.7 ng/L	TMX-049 200 mg	19	0.46 (0.26, 0.82)	
	TMX-049 40 mg	25	0.83 (0.49, 1.43)	
	Placebo	21	-	
8-OHdG < 6.8 nmol/L/mg/dL	TMX-049 200 mg	19	1.03 (0.56, 1.89)	0.375
	TMX-049 40 mg	15	1.12 (0.58, 2.14)	
	Placebo	12	-	
8-OHdG >= 6.8 nmol/L/mg/dL	TMX-049 200 mg	15	0.53 (0.24, 1.15)	
	TMX-049 40 mg	17	0.88 (0.41, 1.89)	
	Placebo	14	-	

8-OHdG, creatinine-corrected 8-hydroxy-2'-deoxyguanosine; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; hsCRP, high-sensitivity C-reactive protein; SBP, systolic blood pressure; sTNFR1, soluble tumor necrosis factor receptor 1; sUA, serum uric acid; UACR, urine albumin-to-creatinine ratio.

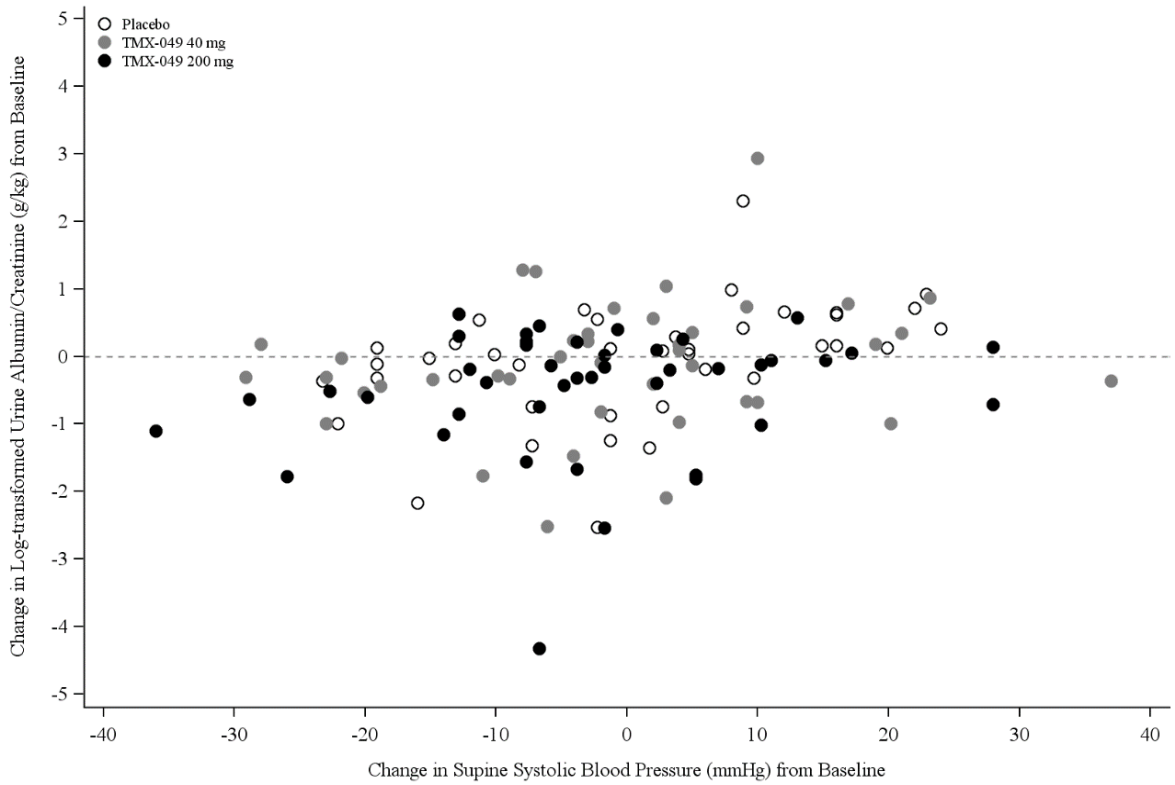
Supplementary Figure 2. Mean change (± standard deviation) in the supine systolic blood pressure from baseline to each study visit.

Data are presented for the safety population (*N*=130): TMX-049 200 mg (*n*=44), TMX-049 40 mg (*n*=44), and placebo (*n*=42). The baseline means of the TMX-049 200 mg, TMX-049 40 mg, and placebo groups were 139, 138, and 137, respectively.



Supplementary Figure 3. Scatter plot of changes in the UACR versus changes in the supine systolic blood pressure from baseline to Week 12.

Data are presented for the modified intention-to-treat population (*N*=129): TMX-049 200 mg (*n*=44), TMX-049 40 mg (*n*=43), and placebo (*n*=42).



UACR, urine albumin-to-creatinine ratio.