



Supplemental Figure: Treatment Duration. Treatment duration is the time from the initial to the final dose of placebo or transforming growth factor- β 1 monoclonal antibody treatment.

Supplemental Table 1: Least Squares Changes from Baseline in Serum Creatinine, First-Morning UPCR and eGFR based on MMRM Analysis Expressed as Percents

Variable	Placebo	TGF- β 1 mAb		
		2 mg	10 mg	50 mg
Serum Creatinine (% change)*				
6 months				
<i>N</i>	89	91	92	87
LS mean	9%	12%	9%	12%
95% CI	(6%, 12.9%)	(8.2%, 15.2%)	(6%, 12.9%)	(8.2%, 15.2%)
Endpoint				
<i>N</i>	85	90	91	82
LS mean	14%	20%	19%	19%
95% CI	(9.7%, 18.2%)	(15.3%, 24.3%)	(14.2%, 23.0%)	(14.0%, 23.3%)
*Back-transformed from log-transformed analysis				
First-Morning UPCR (% change)*				
6 months				
<i>N</i>	88	92	94	90
LS mean	-9%	-2%	-4%	-8%
95% CI	(-19.7%, 4%)	(-13.4%, 10.9%)	(-15.1%, 8.7%)	(-18.6%, 4.6%)
Endpoint				
<i>N</i>	82	87	85	81
LS mean	6%	5%	5%	-1%
95% CI	(-8.5%, 23.2%)	(-8.7%, 21.1%)	(-8.9%, 21.3%)	(-14.5%, 14.7%)

*Back-transformed from log-transformed analysis

eGFR (% change)**

6 months

<i>n</i>	89	91	92	87
LS mean	-8%	-12%	-8%	-10%
95% CI	(-11.1%, -4.9%)	(-14.6%, -8.5%)	(-11.2%, -5.1%)	(-13.4%, -7.1%)

Endpoint

<i>n</i>	85	90	91	82
LS mean	-11%	-17%	-15%	-14%
95% CI	(-14.8%, -7.1%)	(-20.2%, -12.9%)	(-18.7%, -11.3%)	(-17.4%, -9.7%)

**Relative to overall baseline

mean = 35.464

Supplemental Table 2: Observed Change from Baseline in Serum Creatinine, First Morning UPCR, and eGFR by Diabetes Type

Variable	Diabetes Type 1 TGF-β1 mAb				Diabetes Type 2 TGF-β1 mAb			
	Placebo	2 mg	10 mg	50 mg	Placebo	2 mg	10 mg	50 mg
Serum Creatinine (% change)								
Baseline								
<i>n</i>	10	12	11	11	93	92	92	93
mean ± SD	2.39 ± 0.6170	2.010 ± 0.5393)	2.097 ± 0.5991)	2.083 ± 0.5368)	2.190 ± 0.5890	2.145 ± 0.5913)	2.090 ± 0.6631	2.137 ± 0.6446
6 months								
<i>n</i>	9	11	7	11	80	79	85	75
mean ± SD	2.81 ± 1.3738	2.04 ± 0.6033	2.28 ± 0.7295	2.37 ± 0.7845	2.40 ± 0.7810	2.43 ± 0.7210	2.36 ± 0.9624	2.48 ± 1.0639
change from baseline	0.545 ± 1.0107	0.157 ± 0.3392	0.351 ± 0.267	0.291 ± 0.4847	0.199 ± 0.4893	0.294 ± 0.4087	0.238 ± 0.4708	0.341 ± 0.6169
Endpoint								
<i>n</i>	8	11	9	11	77	79	82	70
mean ± SD	2.888 ± 1.7714	2.326 ± 0.9012)	2.464 ± 1.0946	2.683 ± 0.9889)	2.449 ± 0.8541	2.523 ± 0.8231	2.553 ± 1.2074	2.440 ± (0.9427)
change from baseline	0.683 ± 1.4361	0.354 ± 0.5053	0.486 ± 0.6056	0.600 ± 0.6401	0.296 ± 0.5409	0.416 ± 0.4734	0.468 ± 0.7821	0.382 ± 0.5638
First-Morning UPCR (% change)*								
Baseline								
<i>n</i>	10	12	11	11	93	92	92	93
mean ± SD	2.973 (2.2463)	2.733 (1.3390)	2.958 (2.9755)	2.549 (1.2113)	3.139 (2.5560)	3.333 (2.7023)	3.342 (2.3968)	3.480 (2.6422)
6 months								
<i>n</i>	10	10	8	11	78	81	86	78
mean ± SD	2.954 (2.1076)	2.463 (1.2339)	1.778 (0.9663)	3.072 (1.6895)	3.035 (2.8583)	4.125 (7.3198)	3.345 (2.6022)	3.572 (3.7607)
change from baseline	-0.018 (1.8416)	-0.228 (0.8209)	-0.451 (0.8750)	0.523 (1.7339)	3.480 (2.6422)	0.784 (6.6378)	-0.027 (1.7016)	0.070 (2.2277)
Endpoint								

<i>n</i>	8	9	8	11	74	78	77	69
mean ± SD	2.853 (2.5507)	2.765 (1.8852)	2.785 (1.2155)	2.519 (1.7709)	3.244 (2.7883)	3.587 (2.7881)	3.732 (3.3913)	3.622 (3.6162)
change from baseline	0.053 (1.6057)	0.347 (2.2653)	0.938 (1.2299)	-0.030 (1.6710)	0.445 (1.7827)	0.301 (2.5662)	0.426 (2.4007)	0.292 (2.3776)
eGFR (% change)**								
Baseline								
<i>n</i>	10	12	11	11	93	92	92	93
mean ± SD	32.925 (10.8296)	39.147 (11.8994)	38.125 (14.8094)	39.714 (13.7695)	33.932 (11.1341)	35.229 (11.7506)	36.147 (12.2901)	35.511 (11.9412)
6 months								
<i>n</i>	9	11	7	11	80	79	85	75
mean ± SD	31.614 (14.9630)	38.656 (13.0290)	34.265 (12.9940)	35.749 (15.8001)	31.206 (11.1442)	30.703 (10.9503)	32.885 (13.1696)	32.027 (12.9026)
change from baseline	-2.884 (6.3190)	-2.091 (5.6400)	-6.788 (3.4189)	-3.965 (7.2730)	-2.463 (5.7121)	-4.483 (5.9590)	-2.757 (5.5784)	-3.890 (5.6290)
Endpoint								
<i>n</i>	8	11	9	11	77	79	82	70
mean ± SD	31.586 (12.4008)	35.076 (13.8327)	34.135 (15.0718)	34.405 (20.7490)	31.197 (12.2165)	30.365 (12.7661)	30.969 (13.4075)	31.922 (12.6396)
change from baseline	-4.779 (5.9044)	-4.856 (10.2746)	-7.058 (4.8196)	-5.309 (17.9751)	-3.240 (5.4473)	-5.448 (5.5920)	-5.197 (7.7911)	-4.733 (6.6155)

Supplemental Table 3: Treatment Effects on Exploratory Plasma Biomarkers

	Baseline			5.5 months			12 months ^b		
Treatment ^a	n	Median	IQR	n	Median	IQR	n	Median	IQR
Cystatin C (ng/mL)									
Placebo	60	2733	1401	46	3040	1547	51	3051	1757
mAb 2 mg	71	2558	1164	51	2831	1787	53	2605	1065
mAb 10 mg	66	2638	1269	49	2900	1192	54	2822	1208
mAb 50 mg	71	2589	1497	49	3055	1193	55	2772	1158
Kidney injury molecule-1 (KIM-1 (ng/mL))									
Placebo	33	0.683	0.773	26	0.770	0.526	24	0.901	0.830
mAb 2 mg	50	0.682	0.701	37	0.451	0.673	32	0.491	1.053
mAb 10 mg	41	0.709	1.171	31	0.866	1.537	33	0.780	0.914
mAb 50 mg	48	0.659	0.729	31	0.759	0.817	30	0.872	0.840
Neutrophil gelatinase-associated lipocalin (NGAL (ng/mL))									
Placebo	61	284.2	212.3	45	374.8	221.6	28	225.5	129.1
mAb 2 mg	74	255.5	247.7	53	279.6	184.6	29	273.2	147.3
mAb 10 mg	68	260.1	202.3	51	337.6	255.2	30	244.1	185.4
mAb 50 mg	75	295.8	205.6	51	317.6	270.8	29	230.1	271.9
Soluble tumor necrosis factor receptor 2 (sTNFR2 (ng/mL))									
Placebo	60	9.77	3.43	46	10.32	2.80	28	10.10	4.58
mAb 2 mg	71	8.68	3.50	48	9.21	3.97	29	8.74	3.03

	Baseline			5.5 months			12 months ^b		
Treatment ^a	n	Median	IQR	n	Median	IQR	n	Median	IQR
mAb 10 mg	67	9.83	2.93	50	9.92	3.43	30	10.14	3.89
mAb 50 mg	72	8.92	4.44	49	9.42	3.71	28	9.34	5.67

Abbreviation: IQR = interquartile range, mAb = monoclonal antibody

^a mAb refers to transforming growth factor- β 1 mAb treatment

^b Last observation after 5.5 months carried forward

Supplemental Table 4: Treatment Effects on Exploratory Urine Biomarkers^a

	Baseline			5.5 months			12 months ^c		
Treatment ^b	n	Median	IQR	n	Median	IQR	n	Median	IQR
Fibronectin (ug/mg)									
Placebo	55	1.613	3.182	43	1.535	2.966	54	2.041	3.853
mAb 2 mg	62	2.117	2.834	48	1.959	2.425	60	2.444	6.294
mAb 10 mg	67	1.662	3.194	52	2.440	3.122	66	1.940	3.406
mAb 50 mg	67	2.235	5.170	47	2.487	5.706	64	2.121	8.114
High Molecular Weight type IV collagen (HMW Collagen IV (ng/mg))									
Placebo	56	28.68	35.97	44	11.67	17.44	55	15.22	18.96
mAb 2 mg	64	16.95	29.10	52	10.53	12.16	62	11.50	22.72
mAb 10 mg	67	16.23	37.10	52	11.07	13.45	66	13.90	15.94
mAb 50 mg	69	19.71	42.04	49	7.98	13.14	66	12.84	21.85
Monocyte chemotactic protein-1 (MCP-1 (pg/mg))									
Placebo	55	399.1	374.4	44	405.9	300.7	54	448.6	693.5
mAb 2 mg	63	572.8	508.0	51	520.2	628.7	61	619.0	644.5
mAb 10 mg	67	458.5	505.6	52	454.3	533.8	66	439.8	573.0
mAb 50 mg	67	443.6	529.1	50	434.9	611.8	64	544.9	758.3
Matrix metalloproteinase-7 (MMP-7 (ng/mg))									
Placebo	54	10.73	12.73	40	10.13	13.29	24	14.23	17.52
mAb 2 mg	62	16.45	18.79	47	15.56	20.20	18	10.96	22.00
mAb 10 mg	66	10.19	15.65	49	12.21	19.03	25	9.64	10.19

	Baseline			5.5 months			12 months ^c		
Treatment ^b	n	Median	IQR	n	Median	IQR	n	Median	IQR
mAb 50 mg	68	9.54	18.94	45	12.09	21.23	25	13.52	22.55

Abbreviation: IQR = interquartile range, mAb = monoclonal antibody

^a Marker adjusted for urine creatinine excretion

^b mAb refers to transforming growth factor- β 1 mAb treatment

^c Last observation after 5.5 months carried forward

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