Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix:

Angiotensin Blockade in Late Autosomal Dominant Polycystic Kidney Disease

Vicente E. Torres MD, PhD; Kaleab Z. Abebe PhD; Arlene B. Chapman MD; Robert W. Schrier MD; William E. Braun MD; Theodore I. Steinman MD; Franz T. Winklhofer MD; Godela Brosnahan MD; Peter G. Czarnecki MD; Marie C. Hogan MD, PhD; Dana C. Miskulin MD; Frederic F. Rahbari-Oskoui MD; Jared J. Grantham MD; Peter C. Harris, PhD; Michael F. Flessner MD, PhD; Charity G. Moore PhD, MSPH; and Ronald D. Perrone MD; for the HALT PKD Trial Investigators.

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HALT-PKD Study Team Members

In addition to the authors, the following investigators participated in the HALT Progression of Polycystic Kidney Disease (HALT PKD) Trials:

Beth Israel Deaconess Medical Center: Theodore Steinman, MD, Jesse Wei, MD, Peter Czarnecki, MD, Ivan Pedrosa, MD; ***Cleveland Clinic Foundation:*** William Braun, MD, Saul Nurko, MD, Erick Remer, MD; ***Emory University:*** Arlene Chapman, MD, Diego Martin, MD, PhD, Frederic Rahbari-Oskoui, MD, MS, Pardeep Mittal, MD; ***Mayo Clinic:*** Vicente Torres, MD, PhD, Marie C. Hogan, MD, PhD, Ziad El-Zoghby, MD, Peter Harris, PhD, James Glockner, MD, PhD, Bernard King Jr, MD; ***Tufts Medical Center:*** Ronald Perrone, MD, Neil Halin, DO, Dana Miskulin, MD; ***University of Colorado:*** Robert Schrier, MD, Godela Brosnahan, MD, Berenice Gitomer, PhD, Cass Kelleher, MD, Amirali Masoumi, MD, Nayana Patel, MD; ***University of Kansas Medical Center:*** Franz Winklhofer, MD, Jared Grantham, MD, Alan Yu, MB, B Chir, Connie Wang, MD, Louis Wetzel, MD; ***University of Pittsburgh (Data Coordinating Center):*** Charity G. Moore, PhD, MSPH, James E. Bost, PhD, Kyongtae Bae, MD, Kaleab Z. Abebe; ***Washington University in St. Louis (Data Coordinating Center):*** J. Philip Miller, PhD, Paul A. Thompson; ***National Institutes of Health (NIH):*** Josephine Briggs, MD, Michael Flessner, MD, Catherine M. Meyers, MD, and Robert Star, MD.

Data and Safety Monitoring Committee: James Shayman, MD, (Chair), William Henrich, MD, (Former Chair), Tom Greene, PhD, Mary Leonard, MD, MSCE, Peter McCullough, MD, PhD, Sharon Moe, MD, Michael Rocco, MD, and David Wendler, PhD.

Figure S1. Achievement of blood pressure targets.

Percent of participants with systolic (Panels A and B), diastolic (Panels C and D) and mean (Panels E and F) blood pressures below, within or above targets in the lisinopril/telmisartan (Panels A, C and E) and lisinopril/placebo (Panels B, D and F) groups.

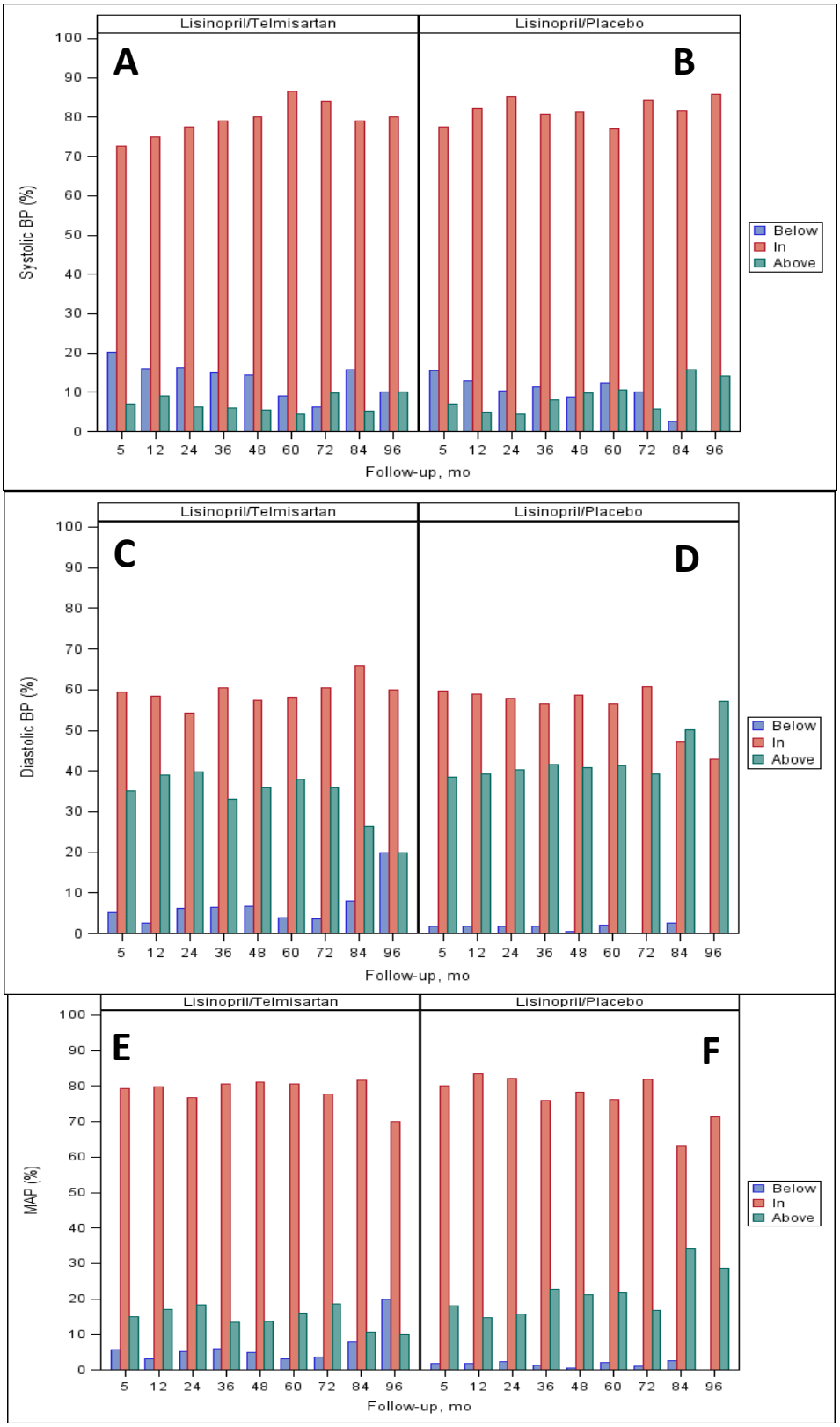

Table S1. Protocol for Addition of Antihypertensive Agents

Step	Telmisartan		Placebo	
1-4	ACE-I	ARB	ACE-I	Placebo
	Lisinopril 5mg	Telmisartan 40 mg	Lisinopril 5mg	Placebo 40 mg
	Lisinopril 10mg	Telmisartan 40 mg	Lisinopril 10mg	Placebo 40 mg
	Lisinopril 20mg	Telmisartan 80 mg	Lisinopril 20mg	Placebo 80 mg
	Lisinopril 40mg	Telmisartan 80 mg	Lisinopril 40mg	Placebo 80 mg
5-6	Furosemide 20 mg - 40 mg BID		Furosemide 20 mg - 40 mg BID	
7-9	Metoprolol 50 mg BID Metoprolol 100 mg BID Metoprolol 200 mg BID		Metoprolol 50 mg BID Metoprolol 100 mg BID Metoprolol 200 mg BID	
10 and onwards	Non-dihydropyridine calcium channel blockers, clonidine, minoxidil, hydralazine at discretion of investigator		Non-dihydropyridine calcium channel blockers, clonidine, minoxidil, hydralazine at discretion of investigator	

Table S2. Additional characteristics of Study B participants at screening or baseline

		Lisinopril/ Telmisartan (n=244)	Lisinopril/ Placebo (n=242)
Measure	**Category**	**n (%)**	**n (%)**
Race*	American Indian or Alaska Native	2 (0.8%)	2 (0.8%)
	Asian	2 (0.8%)	5 (2.1%)
	Black or African American	5 (2.0%)	7 (2.9%)
	White or Caucasian	230 (94.3%)	224 (92.6%)
	Some Other Race	4 (1.6%)	4 (1.7%)
Highest education level	Some high school	0 (0.0%)	2 (0.8%)
	Completed HS or Equivalent	31 (12.8%)	22 (9.1%)
	Some college	62 (25.6%)	55 (22.7%)
	Completed college	74 (30.6%)	86 (35.5%)
	Graduate studies	75 (31.0%)	77 (31.8%)
Marital status	Single	24 (9.9%)	28 (11.6%)
	Married	189 (77.8%)	174 (71.9%)
	Divorced	23 (9.5%)	30 (12.4%)
	Separated	1 (0.4%)	3 (1.2%)
	Widowed	5 (2.1%)	3 (1.2%)
	Other	1 (0.4%)	4 (1.7%)
Employment*	Student	5 (2.0%)	6 (2.5%)
	Homemaker	17 (7.0%)	26 (10.7%)
	Retired	18 (7.4%)	21 (8.7%)
	Disabled	5 (2.0%)	4 (1.7%)
	Full-Time Employment	169 (69.3%)	173 (71.5%)
	Part-Time Employment	31 (12.7%)	19 (7.9%)
	Other	7 (2.9%)	5 (2.1%)
Diagnosis due to	Screening	96 (39.3%)	88 (36.4%)
	Hypertension	32 (13.1%)	37 (15.3%)
	Other	30 (12.3%)	35 (14.5%)
	Pain	30 (12.3%)	22 (9.1%)
	Incidental imaging	23 (9.4%)	24 (9.9%)
	Hematuria	13 (5.3%)	20 (8.3%)
	Routine physical	15 (6.1%)	12 (5.0%)
	UTI	5 (2.0%)	4 (1.7%)
Diagnosis of ADPKD, Mode	Ultrasound	174 (71.3%)	177 (73.1%)
	CT	29 (11.9%)	25 (10.3%)
	IVP	15 (6.1%)	16 (6.6%)
	MRI	12 (4.9%)	11 (4.5%)
	Unknown	5 (2.0%)	5 (2.1%)
	X-Ray	5 (2.0%)	4 (1.7%)

		Lisinopril/ Telmisartan (n=244)	Lisinopril/ Placebo (n=242)
Measure	**Category**	**n (%)**	**n (%)**
	Other	2 (0.8%)	4 (1.7%)
	Angiogram	2 (0.8%)	0 (0.0%)
Family History of ADPKD, no. (%)		214 (87.7)	212 (87.6)
Antihypertensive medication use at Screening			
	Any ARB	61 (25.4%)	57 (23.8%)
	Any Ace Inhibitor	132 (55.0%)	133 (55.6%)
	Any Alpha Blocker	17 (7.1%)	16 (6.7%)
	Any Beta Blocker	47 (19.6%)	49 (20.5%)
	Any Calcium Blocker	40 (16.7%)	35 (14.6%)
	Any Diuretic	48 (20.0%)	42 (17.6%)
Measure		**Mean ± SD**	**Mean ± SD**
Age at diagnosis of ADPKD (yrs)		33.0 ± 12.0	33.5 ± 12.4
Age at diagnosis of HTN (yrs)		36.2 ± 10.2	36.7 ± 10.2
Height (cm)		173.2 ± 10.5	173.1 ± 10.4
BSA (m^2)		2.0 ± 0.2	2.0 ± 0.3
Office systolic BP at screening (mmHg)[§]		123.2 ± 16.2	119.7 ± 14.8
Office diastolic BP at screening (mmHg)		76.3 ± 11.6	75.5 ± 10.2
Office MAP at screening (mmHg)		92.0 ± 12.1	90.2 ± 10.7
Hemoglobin (g/dL)		13.8 ± 1.4	13.7 ± 1.5
S. sodium (mEq/L)		139.4 ± 2.5	139.5 ± 2.3
S. potassium (mEq/L)		4.3 ± 0.5	4.3 ± 0.5
Urea Nitrogen (BUN) mg/dL		24.4 ± 7.5	24.4 ± 7.6
Total CO2 mEq/L or mmol/L		26.2 ± 2.6	26.5 ± 2.4
Urine volume (ml/24 hrs)		2684 ± 1047	2686 ± 1100
Urine potassium (mEq/24 hrs)		64.6 ± 27.9	60.6 ± 24.9

*Some participants selected >1 category; †p-value on the comparison of the transformed variable

[§] P<0.05 for the comparison between lisinopril/telmisartan and lisinopril/placebo.

Table S3: Home and office blood pressures, heart rates, medication steps, and doses of lisinopril and telmisartan/placebo at baseline and study visits.

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
Measure	**Timepoint**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
Home average systolic BP (mmHg)	B1	187	125.4 ± 11.3	184	123.7 ± 10.3
	F5	207	115.9 ± 7.9	218	117.5 ± 8.6
	F12	204	116.7 ± 7.8	210	117.9 ± 6.7
	F18	200	117.4 ± 6.7	205	118.4 ± 7.6
	F24	194	117.2 ± 7.1	207	118.9 ± 6.9
	F30	188	118.4 ± 7.2	197	119.3 ± 7.9
	F36	181	117.2 ± 6.9	196	119.0 ± 8.2
	F42	174	118.3 ± 6.8	172	119.6 ± 7.7
	F48	159	117.4 ± 7.0	162	119.4 ± 8.1
	F54	150	119.1 ± 7.6	145	120.1 ± 8.7
	F60	130	118.3 ± 6.0	129	119.1 ± 8.1
	F66	107	119.9 ± 6.8	103	120.1 ± 8.4
	F72	70	118.5 ± 7.0	84	119.2 ± 7.3
	F78	54	120.3 ± 7.3	55	120.7 ± 8.4
	F84	32	120.0 ± 6.1	33	123.0 ± 8.0
	F90	18	121.1 ± 5.7	18	123.3 ± 14.0
	F96	8	122.3 ± 9.0	7	121.2 ± 7.8
Home average diastolic BP (mmHg)	B1	187	82.1 ± 8.4	184	81.5 ± 7.8
	F5	207	77.7 ± 6.6	219	78.9 ± 6.3
	F12	204	78.2 ± 6.4	210	78.9 ± 5.4
	F18	200	78.7 ± 6.5	205	79.0 ± 5.7
	F24	194	78.4 ± 6.9	207	79.2 ± 5.5
	F30	189	78.7 ± 6.2	197	79.3 ± 6.1
	F36	181	77.9 ± 6.3	196	79.1 ± 6.0
	F42	174	78.4 ± 6.0	172	79.2 ± 6.0
	F48	159	77.5 ± 6.8	162	79.0 ± 5.8
	F54	150	78.8 ± 6.3	145	79.4 ± 5.9
	F60	130	78.5 ± 6.3	129	79.1 ± 5.9
	F66	107	79.3 ± 6.4	103	79.2 ± 5.7
	F72	70	78.1 ± 7.1	84	79.2 ± 5.1
	F78	54	78.4 ± 6.2	55	80.1 ± 5.5
	F84	32	76.7 ± 6.0	33	80.0 ± 5.6
	F90	18	74.9 ± 5.1	18	78.6 ± 6.5
	F96	8	74.4 ± 7.5	7	81.3 ± 6.3
Home average heart rate (bpm)	B1	178	65.5 ± 9.5	172	65.2 ± 9.6
	F5	197	69.9 ± 10.1	213	68.2 ± 9.7

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
Measure	**Timepoint**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
	F12	193	69.3 ± 9.6	204	68.1 ± 9.7
	F18	191	68.6 ± 9.2	196	67.9 ± 9.3
	F24	189	68.2 ± 9.0	201	67.4 ± 9.7
	F30	182	68.7 ± 9.1	194	68.1 ± 9.7
	F36	176	69.4 ± 10.0	188	67.0 ± 9.3
	F42	169	68.8 ± 9.8	165	67.3 ± 9.9
	F48	153	69.1 ± 9.7	158	67.3 ± 9.3
	F54	145	68.7 ± 9.0	140	67.8 ± 10.2
	F60	128	69.3 ± 9.3	122	67.3 ± 9.4
	F66	104	69.4 ± 10.4	100	67.8 ± 9.7
	F72	66	70.8 ± 10.4	77	68.5 ± 10.3
	F78	52	69.4 ± 9.7	54	68.9 ± 10.1
	F84	31	69.2 ± 10.0	32	67.0 ± 9.9
	F90	17	66.3 ± 9.0	18	68.6 ± 10.2
	F96	8	70.5 ± 8.9	7	75.4 ± 12.9
Home average MAP (mmHg)	B1	187	96.5 ± 8.4	184	95.5 ± 7.8
	F5	207	90.4 ± 6.0	218	91.7 ± 6.2
	F12	204	91.0 ± 5.9	210	91.9 ± 4.9
	F18	200	91.6 ± 5.6	205	92.1 ± 5.4
	F24	194	91.3 ± 6.0	207	92.4 ± 5.1
	F30	188	92.0 ± 5.5	197	92.7 ± 5.8
	F36	181	91.0 ± 5.4	196	92.4 ± 5.7
	F42	174	91.7 ± 5.1	172	92.7 ± 5.5
	F48	159	90.8 ± 5.9	162	92.4 ± 5.4
	F54	150	92.2 ± 5.8	145	92.9 ± 5.8
	F60	130	91.8 ± 5.3	129	92.4 ± 5.5
	F66	107	92.8 ± 5.4	103	92.8 ± 5.6
	F72	70	91.6 ± 5.8	84	92.5 ± 4.9
	F78	54	92.4 ± 5.2	55	93.6 ± 5.6
	F84	32	91.1 ± 4.9	33	94.3 ± 4.9
	F90	18	90.3 ± 3.8	18	93.5 ± 7.9
	F96	8	90.4 ± 7.7	7	94.6 ± 6.1
Office average systolic BP (mmHg)	B1	244	129.8 ± 14.3	240	128.3 ± 14.8
	F5	227	116.9 ± 12.9	231	119.4 ± 12.7
	F12	222	118.5 ± 12.2	222	118.6 ± 12.1
	F18	212	119.2 ± 11.5	223	120.3 ± 12.9
	F24	208	118.5 ± 11.3	221	119.6 ± 11.7
	F30	198	120.1 ± 11.9	206	121.5 ± 13.4
	F36	196	120.2 ± 12.1	209	121.2 ± 11.8
	F42	172	120.9 ± 11.7	184	120.5 ± 12.7
	F48	176	119.7 ± 11.5	178	120.7 ± 12.2

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
Measure	**Timepoint**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
	F54	163	120.3 ± 11.3	149	122.0 ± 11.9
	F60	150	121.6 ± 10.7	148	121.7 ± 12.4
	F66	119	122.2 ± 10.0	115	122.6 ± 12.7
	F72	81	124.1 ± 12.0	88	124.2 ± 12.0
	F78	65	126.9 ± 16.3	59	121.8 ± 11.6
	F84	36	124.5 ± 13.1	37	124.4 ± 11.8
	F90	24	125.6 ± 13.5	21	120.9 ± 14.8
	F96	9	128.2 ± 11.4	7	115.1 ± 6.7
Office average diastolic BP (mmHg)	B1	244	79.7 ± 10.6	240	79.1 ± 9.7
	F5	227	72.8 ± 10.4	231	75.3 ± 8.9
	F12	222	74.6 ± 9.8	222	75.5 ± 9.2
	F18	212	75.4 ± 9.4	223	76.7 ± 9.3
	F24	208	75.0 ± 9.5	221	76.6 ± 7.8
	F30	198	76.3 ± 9.0	206	78.0 ± 8.7
	F36	196	76.2 ± 9.3	209	77.5 ± 8.6
	F42	172	76.9 ± 8.6	184	77.4 ± 8.1
	F48	176	76.2 ± 8.7	178	77.5 ± 9.2
	F54	163	76.9 ± 9.9	149	78.9 ± 9.3
	F60	150	77.1 ± 8.4	148	77.9 ± 8.4
	F66	119	76.3 ± 8.0	115	78.1 ± 9.2
	F72	81	76.3 ± 9.4	88	80.3 ± 8.4
	F78	65	77.5 ± 9.9	59	79.0 ± 8.3
	F84	36	75.4 ± 7.5	37	77.8 ± 8.7
	F90	24	74.4 ± 6.5	21	75.7 ± 9.4
	F96	9	73.9 ± 10.6	7	73.2 ± 8.0
Office average heart rate (bpm)	B1	234	64.3 ± 11.3	235	63.8 ± 10.3
	F5	223	69.2 ± 12.0	227	67.4 ± 13.0
	F12	221	69.6 ± 12.7	222	68.7 ± 12.4
	F18	211	68.6 ± 11.6	222	68.2 ± 13.2
	F24	206	67.8 ± 11.5	220	67.9 ± 12.9
	F30	197	67.6 ± 11.7	203	66.6 ± 12.2
	F36	194	68.6 ± 12.1	209	67.3 ± 12.7
	F42	171	67.5 ± 11.6	183	66.3 ± 12.0
	F48	176	69.0 ± 12.3	178	66.7 ± 12.1
	F54	163	68.3 ± 10.6	149	67.0 ± 12.4
	F60	150	69.4 ± 11.6	147	67.1 ± 11.7
	F66	119	68.5 ± 10.1	115	66.2 ± 12.5
	F72	81	68.7 ± 11.1	88	66.5 ± 11.2
	F78	65	67.0 ± 10.3	58	68.6 ± 12.3
	F84	35	67.3 ± 10.8	36	63.7 ± 12.6
	F90	24	65.9 ± 14.3	21	66.1 ± 10.1

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
Measure	**Timepoint**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
	F96	9	63.4 ± 10.3	7	74.6 ± 13.8
Office average MAP (mmHg)	B1	244	96.4 ± 10.6	240	95.5 ± 10.3
	F5	227	87.5 ± 10.4	231	90.0 ± 9.1
	F12	222	89.2 ± 9.3	222	89.9 ± 9.2
	F18	212	90.0 ± 9.0	223	91.2 ± 9.6
	F24	208	89.5 ± 9.1	221	90.9 ± 8.0
	F30	198	90.9 ± 9.1	206	92.5 ± 9.1
	F36	196	90.9 ± 9.2	209	92.1 ± 8.5
	F42	172	91.6 ± 8.6	184	91.8 ± 8.7
	F48	176	90.7 ± 8.4	178	91.9 ± 9.0
	F54	163	91.4 ± 9.6	149	93.3 ± 9.2
	F60	150	91.9 ± 7.8	148	92.5 ± 8.5
	F66	119	91.6 ± 7.5	115	92.9 ± 9.3
	F72	81	92.2 ± 9.0	88	95.0 ± 8.7
	F78	65	93.9 ± 10.9	59	93.3 ± 8.5
	F84	36	91.7 ± 8.5	37	93.3 ± 8.8
	F90	24	91.5 ± 7.6	21	90.8 ± 10.9
	F96	9	92.0 ± 9.3	7	87.2 ± 7.1

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
Measure	**Timepoint**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
BP Step	B1	225	1.4 ± 0.7	222	1.3 ± 0.7
	F12	216	2.8 ± 2.4	218	3.2 ± 2.3
	F24	208	3.0 ± 2.5	213	3.3 ± 2.4
	F36	189	2.9 ± 2.5	200	3.4 ± 2.6
	F48	172	2.8 ± 2.4	174	3.3 ± 2.5
	F60	144	2.7 ± 2.2	142	3.1 ± 2.4
	F72	75	2.3 ± 1.9	87	2.7 ± 2.2
	F84	33	2.3 ± 2.1	35	2.9 ± 2.6
	F96	8	1.1 ± 1.6	7	1.7 ± 2.0
Lisinopril dose (mg/day)	B1	222	6.9 ± 4.9	214	6.6 ± 4.6
	F12	176	17.7 ± 15.7	204	19.6 ± 15.8
	F24	172	16.7 ± 15.0	194	19.1 ± 15.1
	F36	154	16.9 ± 15.9	183	17.8 ± 15.3
	F48	135	15.1 ± 14.7	163	17.9 ± 15.4
	F60	113	14.7 ± 14.0	130	17.1 ± 16.1
	F72	59	15.2 ± 14.2	81	13.8 ± 14.5
	F84	24	15.9 ± 15.0	28	18.7 ± 16.4

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
Measure	**Timepoint**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
	F96	3	14.2 ± 22.4	6	14.2 ± 15.6
Telmisartan/Placebo dose (mg/day)*	B1	220	41.0 ± 6.0	214	40.9 ± 6.1
	F12	205	54.3 ± 21.0	209	58.3 ± 20.1
	F24	195	53.2 ± 21.2	203	58.7 ± 20.4
	F36	176	53.1 ± 20.7	184	57.7 ± 20.2
	F48	162	51.6 ± 21.4	163	56.9 ± 20.7
	F60	131	47.8 ± 24.8	132	54.1 ± 21.2
	F72	68	46.0 ± 23.2	77	45.7 ± 27.3
	F84	29	43.4 ± 25.1	32	43.1 ± 26.0
	F96	7	17.1 ± 21.4	6	6.7 ± 16.3

*Thirty (86%) of the 35 participants that discontinued study drug before the end of follow-up did so due to the following reasons: hypertension, hypotension, hyperkalemia, or intolerable side effects. The remaining 5 did not specify a reason.

Table S4: Percentage of patients on medication step ≤4 by treatment group and visit.

	Lisinopril/Telmisartan (n=244)		Lisinopril/Placebo (n = 242)	
Timepoint	**n**	**(%)**	**n**	**(%)**
B1	225	100%	222	99%
F5	217	77%	226	79%
F12	216	77%	218	75%
F18	213	76%	215	74%
F24	208	75%	213	72%
F30	200	77%	209	71%
F36	189	78%	200	73%
F42	187	77%	185	72%
F48	172	78%	174	71%
F54	158	78%	155	72%
F60	144	81%	142	72%
F66	116	84%	113	76%
F72	75	85%	87	80%
F78	63	86%	57	79%
F84	33	88%	35	80%
F90	20	90%	20	85%
F96	8	88%	7	86%

Table S5A: Percentage of patients categorized by dose of lisinopril*, treatment group and visit.

		Lisinopril/Telmisartan				Lisinopril/Placebo				
Visit	**N**	**5mg**	**10 mg**	**20 mg**	**40 mg**	**5mg**	**10 mg**	**20 mg**	**40 mg**	**P**
B1	422	160 (73.4%)	50 (22.9%)	5 (2.3%)	3 (1.4%)	156 (76.5%)	39 (19.1%)	7 (3.4%)	2 (1.0%)	0.69
F12	272	37 (30.1%)	21 (17.1%)	12 (9.8%)	53 (43.1%)	38 (25.5%)	21 (14.1%)	28 (18.8%)	62 (41.6%)	0.20
F24	255	37 (30.6%)	21 (17.4%)	19 (15.7%)	44 (36.4%)	35 (26.1%)	24 (17.9%)	20 (14.9%)	55 (41.0%)	0.84
F36	226	30 (30.0%)	15 (15.0%)	17 (17.0%)	38 (38.0%)	29 (23.0%)	29 (23.0%)	18 (14.3%)	50 (39.7%)	0.36
F48	192	24 (28.9%)	13 (15.7%)	17 (20.5%)	29 (34.9%)	24 (22.0%)	18 (16.5%)	22 (20.2%)	45 (41.3%)	0.70
F60	152	22 (32.8%)	12 (17.9%)	13 (19.4%)	20 (29.9%)	23 (27.1%)	15 (17.6%)	15 (17.6%)	32 (37.6%)	0.76
F72	82	9 (25.7%)	6 (17.1%)	10 (28.6%)	10 (28.6%)	15 (31.9%)	10 (21.3%)	7 (14.9%)	15 (31.9%)	0.51
F84	34	5 (33.3%)	1 (6.7%)	4 (26.7%)	5 (33.3%)	2 (10.5%)	5 (26.3%)	3 (15.8%)	9 (47.4%)	0.18
F96	5	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100%)	1 (25.0%)	0 (0.0%)	2 (50.0%)	1 (25.0%)	>0.99

* participants with daily doses other than 5, 10, 20 or 40 mg are not included

Table S5B: Percentage of patients categorized by dose of telmisartan/placebo*, treatment group and visit.

		Lisinopril/Telmisartan		Lisinopril/Placebo		
Timepoint	**Frequency**	**40 mg**	**80 mg**	**40 mg**	**80 mg**	**P**
B1	432	213 (97.7%)	5 (2.3%)	209 (97.7%)	5 (2.3%)	0.98
F12	406	126 (63.6%)	72 (36.4%)	112 (53.8%)	96 (46.2%)	0.05
F24	385	113 (61.4%)	71 (38.6%)	105 (52.2%)	96 (47.8%)	0.07
F36	348	103 (62.0%)	63 (38.0%)	100 (54.9%)	82 (45.1%)	0.18
F48	308	93 (62.8%)	55 (37.2%)	89 (55.6%)	71 (44.4%)	0.20
F60	235	65 (60.7%)	42 (39.3%)	78 (60.9%)	50 (39.1%)	0.98
F72	121	39 (68.4%)	18 (31.6%)	40 (62.5%)	24 (37.5%)	0.50
F84	50	17 (70.8%)	7 (29.2%)	18 (69.2%)	8 (30.8%)	>0.99
F96	4	3 (100%)	0 (0.0%)	1 (100%)	0 (0.0%)	**

*** Participants with daily doses other than 40 or 80 mg are not included**

**** P-value was not calculated as there were no participants taking 80 mg at F96.**

Table S6: Open label anti-hypertensive agents added at any time after maximal doses of lisinopril and telmisartan/placebo

Measure	Lisinopril/ Telmisartan (n=244)	Lisinopril/ Placebo (n=242)	
	n (%)	n (%)	p value
Diuretic	92 (37.7%)	113 (46.7%)	0.04
Beta- or alpha/beta blocker	56 (23.0%)	75 (31.0%)	0.05
Calcium channel blocker	36 (14.8%)	44 (18.2%)	0.31
Central alpha 2 adrenergic agonist	15 (6.1%)	21 (8.7%)	0.29
Vasodilator	8 (3.3%)	12 (5.0%)	0.35
Alpha 1 adrenergic receptor blocker	1 (0.4%)	7 (2.9%)	0.03

Table S7A: Secondary outcomes of eGFR, urine albumin excretion, frequencies of PKD related symptoms, pain, and quality of life. Participants were asked about the occurrence of symptoms during the prior 3 months at every study visit per protocol.

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
		n	**Mean ± SD**	**n**	**Mean ± SD**
CKD EPI eGFR (ml/min/1.73m^2)	B1	244	48.5 ± 11.5	242	47.9 ± 12.2
	F5	226	46.5 ± 11.8	231	46.0 ± 12.0
	F12	222	44.0 ± 12.8	222	43.3 ± 12.9
	F18	216	42.4 ± 13.6	222	41.3 ± 13.6
	F24	208	40.8 ± 12.9	221	40.4 ± 14.5
	F30	205	38.9 ± 13.1	212	39.0 ± 15.3
	F36	198	38.6 ± 13.3	211	37.5 ± 14.8
	F42	185	37.2 ± 13.1	187	36.6 ± 14.4
	F48	179	37.0 ± 13.5	182	35.7 ± 13.7
	F54	167	35.8 ± 12.8	156	36.3 ± 13.7
	F60	153	36.2 ± 12.9	150	35.9 ± 13.2
	F66	121	35.8 ± 12.2	115	36.0 ± 13.7
	F72	82	37.6 ± 11.4	90	36.5 ± 12.1
	F78	64	37.1 ± 11.8	59	35.8 ± 12.2
	F84	36	35.2 ± 11.5	37	36.6 ± 12.1
	F90	24	36.9 ± 10.2	21	37.2 ± 13.6
	F96	10	34.1 ± 8.8	7	35.7 ± 12.5
		n	**Median (25th , 75th)**	**n**	**Median (25th , 75th)**
Urine albumin (mg/24 hrs)	B1	237	29.7 (16.6, 71.8)	225	28.1 (17.3, 78.0)
	F5	214	27.1 (14.0, 51.2)	220	27.4 (17.1, 55.0)
	F12	208	22.6 (13.1, 56.0)	199	30.7 (15.0, 54.0)
	F24	184	22.9 (10.3, 59.0)	190	29.7 (13.7, 63.7)
	F36	166	27.7 (13.5, 72.1)	187	34.8 (14.6, 92.9)

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
	F48	159	28.2 (12.7, 73.9)	164	32.8 (13.2, 86.2)
	F60	140	36.2 (14.0, 104.8)	140	28.1 (15.3, 83.5)
	F72	75	34.2 (15.7, 100.3)	84	29.2 (13.3, 56.3)
	F84	34	48.6 (24.4, 111.2)	37	33.0 (13.3, 125.4)
	F96	9	39.2 (12.8, 80.3)	7	61.0 (22.8, 115.3)
		n	**%**	**n**	**%**
Kidney Pain (Back or Flank Pain)	B1	93	38.11	74	30.96
	F12	101	45.70	99	44.39
	F24	99	46.70	102	46.15
	F36	85	42.71	88	42.31
	F48	82	45.81	79	42.93
	F60	69	45.10	64	43.24
	F72	38	46.91	34	37.78
	F84	14	37.84	10	27.03
	F96	2	22.22	2	28.57
Blood in Urine/Hematuria	B1	9	3.69	8	3.33
	F12	15	6.79	18	8.07
	F24	14	6.57	16	7.17
	F36	9	4.50	24	11.43
	F48	14	7.73	11	5.98
	F60	9	5.88	9	5.96
	F72	1	1.22	4	4.44
	F84	1	2.70	2	5.41
	F96	0	0.00	2	28.57
Urinary tract infection	B1	5	2.05	5	2.08
	F12	14	6.39	9	4.04
	F24	7	3.29	15	6.73

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
	F36	9	4.50	8	3.81
	F48	7	3.87	11	5.98
	F60	8	5.23	9	5.96
	F72	1	1.22	5	5.56
	F84	0	0.00	3	8.11
	F96	0	0.00	0	0.00
Kidney stone(s)	B1	2	0.82	5	2.09
	F12	6	2.73	8	3.59
	F24	2	0.94	4	1.79
	F36	0	0.00	4	1.90
	F48	5	2.76	4	2.17
	F60	1	0.65	2	1.32
	F72	1	1.22	3	3.33
	F84	0	0.00	1	2.70
	F96	0	0.00	0	0.00
Experienced back pain in past 3 months	B1	189	80.77	179	76.50
	F12	177	81.94	166	74.77
	F24	159	76.08	173	78.28
	F36	157	78.89	151	72.60
	F48	133	73.89	138	74.59
	F60	109	71.24	112	74.17
	F72	59	71.95	55	61.80
	F84	26	72.22	24	66.67
	F96	4	44.44	3	42.86
Experienced radiating pain in past 3 months	B1	78	33.91	66	28.21
	F12	83	39.15	62	28.05
	F24	59	28.64	76	34.70

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
	F36	62	31.96	72	35.64
	F48	58	33.33	47	25.82
	F60	44	29.73	46	30.87
	F72	28	35.00	23	27.06
	F84	8	21.62	8	22.22
	F96	0	0.00	1	14.29
Experienced abdominal pain in past 3 months	B1	117	50.43	102	43.59
	F12	96	44.86	104	47.27
	F24	101	48.56	110	49.55
	F36	104	52.79	99	48.29
	F48	88	49.44	89	48.37
	F60	79	53.02	70	46.98
	F72	44	55.00	35	40.23
	F84	15	40.54	15	40.54
	F96	4	50.00	3	42.86
		n	**Mean ± SD**	**n**	**Mean ± SD**
SF36v2 Physical Component	B1	238	50.3 ± 8.0	238	50.5 ± 8.3
	F12	216	50.2 ± 7.5	222	50.6 ± 7.9
	F24	206	49.9 ± 8.5	221	49.6 ± 8.7
	F36	197	49.4 ± 8.6	206	49.4 ± 9.2
	F48	179	49.2 ± 9.3	183	48.1 ± 9.8
	F60	148	47.9 ± 9.8	149	48.0 ± 10.9
	F72	82	46.7 ± 10.9	89	48.1 ± 10.5
	F84	36	48.4 ± 9.9	37	50.1 ± 7.9
	F96	8	45.4 ± 14.3	7	52.9 ± 5.0
SF36v2 Mental Component	B1	238	52.1 ± 9.1	238	51.8 ± 8.6
	F12	216	51.8 ± 8.7	222	52.3 ± 8.4

		Lisinopril/ Telmisartan (n=244)		Lisinopril/ Placebo (n=242)	
	F24	206	52.1 ± 9.2	221	52.2 ± 8.5
	F36	197	52.4 ± 9.2	206	52.1 ± 8.2
	F48	179	51.8 ± 9.5	183	51.9 ± 8.8
	F60	148	52.3 ± 9.3	149	51.8 ± 8.4
	F72	82	51.9 ± 9.2	89	53.2 ± 6.7
	F84	36	53.0 ± 7.7	37	53.4 ± 7.4
	F96	8	54.5 ± 7.5	7	54.5 ± 7.6

Table S7B: Results of models testing secondary outcomes of eGFR, urine albumin excretion, frequencies of PKD related symptoms, pain, and quality of life. Below are per-month slopes (unless otherwise specified) along with corresponding p-values. Differences in slopes between Lisinopril/telmisartan and Lisinopril/placbo are also estimated and assessed for significance. For continuous outcomes (eGFR, urine albumin, PCS, and MCS), the slopes are presented as a per-month or per-year increase in the outcome; for binary outcomes, the slopes are presented as a per-month change in the odds of the outcome.

Outcome	Label	Estimate/OR	Lower CL	Upper CL	p value
CKD EPI eGFR (ml/min/1.73m^2)	Lisinopril/placebo slope (per yr)	-3.9074	-4.1693	-3.6454	<.0001
	Lisinopril/telmisartan slope (per yr)	-3.8735	-4.1394	-3.6076	<.0001
	Lisinopril/telmisartan vs Lisinopril/placebo	0.0339	-0.3396	0.4074	0.8585
Log Urine Albumin (mg/24 hrs)	Lisinopril/placebo slope	0.0060	0.0042	0.0079	<.0001
	Lisinopril/telmisartan slope	0.0059	0.0040	0.0077	<.0001
	Lisinopril/telmisartan vs Lisinopril/placebo	-0.0002	-0.0027	0.0023	0.8806
Kidney Pain (Back or Flank Pain)	Lisinopril/placebo slope	1.01	1.01	1.01	<.0001
	Lisinopril/telmisartan slope	1.01	1.00	1.01	0.0002
	Lisinopril/telmisartan vs Lisinopril/placebo	1.00	0.99	1.00	0.6423
Blood in Urine/Hematuria	Lisinopril/placebo slope	1.01	1.00	1.01	0.0874
	Lisinopril/telmisartan slope	1.00	1.00	1.01	0.5670
	Lisinopril/telmisartan vs Lisinopril/placebo	1.00	0.99	1.00	0.3433
Urinary Tract Infection	Lisinopril/placebo slope	1.01	1.00	1.01	0.1233
	Lisinopril/telmisartan slope	1.00	0.99	1.01	0.5482
	Lisinopril/telmisartan vs Lisinopril/placebo	1.00	0.99	1.01	0.4375
Kidney stone(s)	Lisinopril/placebo slope	1.00	0.99	1.01	0.7673

Outcome	Label	Estimate/OR	Lower CL	Upper CL	p value
	Lisinopril/telmisartan slope	0.99	0.98	1.00	0.0483
	Lisinopril/telmisartan vs Lisinopril/placebo	0.99	0.97	1.00	0.0647
Experienced back pain in past 3 months	Lisinopril/placebo slope	0.99	0.99	1.00	0.0171
	Lisinopril/telmisartan slope	0.99	0.99	1.00	0.0045
	Lisinopril/telmisartan vs Lisinopril/placebo	1.00	0.99	1.01	0.6378
Experienced radiating pain in past 3 months	Lisinopril/placebo slope	1.00	0.99	1.01	0.8228
	Lisinopril/telmisartan slope	1.00	0.99	1.00	0.6308
	Lisinopril/telmisartan vs Lisinopril/placebo	1.00	0.99	1.01	0.8404
Experienced abdominal pain in past 3 months	Lisinopril/placebo slope	1.00	1.00	1.01	0.1099
	Lisinopril/telmisartan slope	1.01	1.00	1.01	0.0066
	Lisinopril/telmisartan vs Lisinopril/placebo	1.00	1.00	1.01	0.3470
SF36 PCS	Lisinopril/placebo slope	-0.0537	-0.0655	-0.0420	<.0001
	Lisinopril/telmisartan slope	-0.0565	-0.0699	-0.0430	<.0001
	Lisinopril/telmisartan vs Lisinopril/placebo	-0.0027	-0.0192	0.0137	0.7462
SF36 MCS	Lisinopril/placebo slope	-0.0026	-0.0156	0.0103	0.6896
	Lisinopril/telmisartan slope	-0.0066	-0.0198	0.0067	0.3324
	Lisinopril/telmisartan vs Lisinopril/placebo	-0.0039	-0.0216	0.0137	0.6628

Table S8: Common symptoms reported by participants (participants were asked about presence of symptoms every 3 months).

	Lisinopril/ Telmisartan (n=244)	Lisinopril/ Placebo (n=242)
Follow-up duration (average years)	5.1	5.2
Symptoms		
Any instances of malaise/feeling ill		
Number of events	918	994
Percent of participants affected	84.4%	85.5%
Any instances of headache		
Number of events	1045	1193
Percent of participants affected	73.8%	79.3%
Any instances of nasal congestion		
Number of events	1220	1076
Percent of participants affected	82.4%	83.5%
Any instances of dizziness/lightheadedness		
Number of events	794	744
Percent of participants affected	75.8%	70.2%
Any instances of cough		
Number of events	860	896
Percent of participants affected	77.9%	76.9%
Any instances of joint pain/aches		
Number of events	1431	1156
Percent of participants affected	77.9%	79.8%
Any instances of kidney pain (back or flank)		
Number of events	1876	1863
Percent of participants affected	84.4%	83.1%

Table S9: Adverse events with potentially increased risk previously found to be associated with study drug

	Lisinopril/ Telmisartan (n=244)	Lisinopril/ Placebo (n=242)
Hyperkalemia – Any		
Number of participants affected	46 (18.9%)	41 (16.9%)
Number of events	70	65
Mild (<5.6 mEq/L)	61	60
Moderate (5.6-6.5 mEq/L)	9	4
Severe (>6.5 mEq/L)	0	1
Acute kidney injury (AKI)		
Number of participants affected	22 (9.0%)	32 (13.2%)
Number of events	31	51
Mild (s. creat. Increase >0.3-1 mg/dl)	10	17
Moderate (s. creat. Increase >1-2 mg/dl)	8	14
Severe (s. creat. Increase >2 mg/dl)	3	4
Cancer (number of participants affected)	9 (3.7%)	7 (2.9%)
Melanoma	0 (0.0%)	2 (0.8%)
Breast	3 (1.2%)	2 (0.8%)
Prostate	2 (0.8%)	1 (0.4%)
Kidney	0 (0%)	1 (0.4%)
Bladder	1 (0.4%)	0 (0%)
Lung	0 (0%)	1 (0.4%)
Other	3 (1.2%)	0 (0%)