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Kidney Functional Magnetic Resonance Imaging and Change in eGFR in Individuals with CKD

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Supplemental Table 1. Kidney functional MRI acquisition parameters

Acquisition parameter	Diffusion-weighted MRI	BOLD MRI
Field of view, mm	400	400
Matrix	192 x 192	192 x 192
Repetition time, ms	3000	61
Echo time, ms	78	4.92 – 39.6; step size 4.92
Bandwidth, Hz/pixel	1532	260
Flip angle	90°	30°
Slice orientation	Coronal	Coronal
Slice thickness, mm	5	5
# Slice	5	5
Averages	5	1
Diffusion factor (b), s/mm²	200, 300, 500, 700, 1000	n/a

Supplemental Table 2. Mean annual eGFR slope by tertiles of baseline kidney functional MRI biomarkers

	Model 1			Model 2			Model 3		
	eGFR slope ^a	95% CI	P for trend	eGFR slope ^a	95% CI	P for trend	eGFR slope ^b	95% CI	P for trend
ADC									
Tertile 1 (0.8 – 1.40)	-2.6	-7.2 – 2.1		-2.6	-7.2 – 2.1		-2.6	-7.1 – 1.9	
Tertile 2 (1.41 – 1.51)	-2.7	-7.3 – 1.9	0.55	-2.7	-7.3 – 1.8	0.50	-2.3	-6.8 – 2.2	0.94
Tertile 3 (1.52 – 1.95)	-1.9	-3.7 – 0.02		-1.8	-3.6 – 0.1		-2.2	-4.0 – -0.4	
R2*									
Tertile 1 (13.1 – 18.9)	-2.6	-4.6 – -0.5		-2.5	-4.5 – -0.5		-2.3	-4.3 – -0.4	
Tertile 2 (18.9 – 21.2)	-3.1	-7.9 – 1.8	0.36	-3.1	-7.9 – 1.7	0.37	-3.2	-7.8 – 1.4	0.52
Tertile 3 (21.2 – 33.3)	-1.3	-6.1 – 3.6		-1.2	-6.0 – 3.6		-1.5	-6.1 – 3.1	

Cortical ADC and R2* are reported in ($\times 10^{-3}$ mm²/s) and (s⁻¹), respectively.

^a This estimate reflects the mean annual eGFR slope for each respective MRI biomarker tertile.

^b This estimate reflects the mean annual eGFR slope for each respective MRI biomarker tertile where natural log transformed UACR is centered around the mean.

Model 1 is unadjusted

Model 2 is adjusted for age, sex, race, diabetes status, treatment group (active treatment vs placebo), study center, baseline hemoglobin, baseline log transformed UACR, and baseline eGFR

Model 3 is model 2 and further adjusts for the interaction of natural log transformed UACR x time

Supplemental Table 3. Association of baseline cortical ADC and cortical R2* with change in eGFR over time

	Model 1		Model 2		Model 3	
	β^a (95% CI)	P	β^a (95% CI)	P	β^a (95% CI)	P
Cortical ADC	1.2 (-0.1 – 2.4)	0.06	1.2 (0.01 – 2.4)	0.05	1.0 (-0.1 – 2.2)	0.09
Cortical R2*	0.4 (-0.7 – 1.6)	0.44	0.4 (-0.7 – 1.5)	0.46	0.4 (-0.7 – 1.4)	0.51

^a The β estimate is the difference in annual eGFR slope (ml/min/1.73m²/year) per 1 SD increase in the MRI biomarker of interest from the respective MRI biomarker x time interaction term. P-values are from the interaction term of each respective MRI biomarker x time. Cortical ADC and R2* are reported in ($\times 10^{-3}$ mm²/s) and (s⁻¹), respectively. Time is measured in years.

Model 1 is unadjusted

Model 2 is adjusted for age, sex, race, diabetes status, treatment group (active treatment vs placebo), study center, baseline hemoglobin, baseline log transformed UACR, and baseline eGFR

Model 3 is model 2 and further adjusts for the interaction of natural log transformed UACR x time

Supplemental Table 4. Associations of whole-kidney ADC, whole-kidney R2*, and medullary R2* with change in eGFR over time

	Model 1		Model 2		Model 3	
	β^a (95% CI)	P	β^a (95% CI)	P	β^a (95% CI)	P
Whole-kidney ADC	1.1 (-0.1 – 2.3)	0.06	1.2 (-0.01 – 2.4)	0.05	1.0 (-0.2 – 2.1)	0.09
Whole-kidney R2*	0.7 (-0.4 – 1.8)	0.22	0.7 (-0.4 – 1.8)	0.23	0.5 (-0.6 – 1.5)	0.41
Medullary R2*	1.0 (-0.2 – 2.2)	0.11	0.9 (-0.2 – 2.1)	0.12	0.5 (-0.7 – 1.7)	0.38

^a The β estimate is the difference in annual eGFR slope (ml/min/1.73m²/year) per 1 SD increase in the MRI biomarker of interest from the respective MRI biomarker x time interaction term. P-values are from the interaction term of each respective MRI biomarker x time. ADC and R2* are reported in (x 10⁻³ mm²/s) and (s⁻¹), respectively. Time is measured in years.

Model 1 is unadjusted

Model 2 is adjusted for age, sex, race, diabetes status, treatment group (active treatment vs placebo), study center, baseline hemoglobin, baseline log transformed UACR, and baseline eGFR

Model 3 is model 2 and further adjusts for the interaction of natural log transformed UACR x time

Supplemental Table 5. Associations of kidney functional MRI measurements with rapid CKD progression

Outcome	No. of Events	Cortical ADC ($\times 10^{-3} \text{ mm}^2/\text{s}$) ^a		Cortical R2* (s^{-1}) ^b	
		Unadjusted	Adjusted*	Unadjusted	Adjusted*
Kidney failure or death	6	2.41 (1.19 – 4.87)	2.37 (1.03 – 5.48)	0.49 (0.18 – 1.36)	0.55 (0.16 – 1.83)
eGFR loss > 3 ml/min/1.73m²/year	25	1.43 (0.93 – 2.21)	1.29 (0.82 – 2.04)	0.80 (0.49 – 1.31)	0.81 (0.48 – 1.37)

eGFR loss was calculated by annual subject-specific eGFR slope from mixed-effects models.

^a Measures of association presented as odds ratio with (95% CI) per 1 standard deviation decrease in cortical ADC.

^b Measures of association presented as odds ratio with (95% CI) per 1 standard deviation increase in cortical R2*.

*Model is adjusted for baseline eGFR and baseline natural log transformed UACR

Supplemental Table 6. Kidney functional MRI measurements by treatment group among participants with baseline and follow-up functional MRI

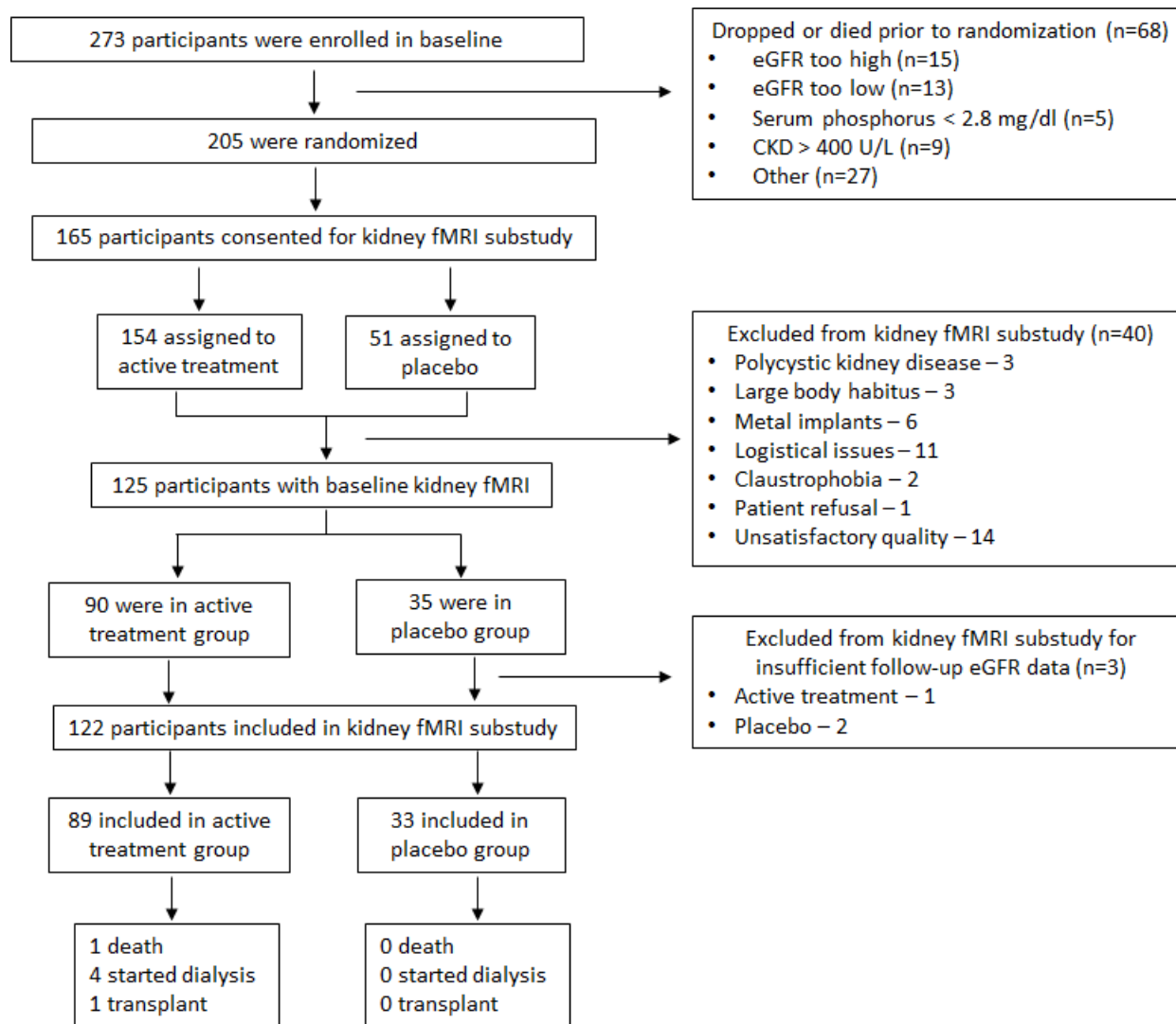
MRI Visit	All patients N = 87	Active Treatment N = 61	Placebo N = 26	P
Cortical ADC (x 10⁻³ mm²/s)				
Baseline	1.46 ± 0.16	1.45 ± 0.16	1.50 ± 0.18	0.21
Month 12	1.49 ± 0.17	1.50 ± 0.17	1.48 ± 0.19	0.64
Δ	0.03 ± 0.13	0.05 ± 0.11	-0.02 ± 0.15	0.02
Cortical R2* (s⁻¹)				
Baseline	20.6 ± 3.4	20.9 ± 3.6	19.8 ± 2.5	0.11
Month 12	20.8 ± 3.1	21.0 ± 3.4	20.2 ± 2.2	0.22
Δ	0.2 ± 2.6	0.1 ± 2.7	0.4 ± 2.4	0.64

Participants in the active treatment group received either lanthanum carbonate and nicotinamide, lanthanum carbonate and nicotinamide placebo, or lanthanum carbonate placebo and nicotinamide. Participants in the placebo group received double placebo treatment.

Data presented as mean ± standard deviation for cortical ADC and R2* measurements at baseline and month 12 visits.

P values compare active treatment vs placebo groups.

Abbreviations: MRI, magnetic resonance imaging



Supplemental Figure 1. Flow diagram for inclusion/exclusion of participants in kidney functional MRI substudy of the COMBINE trial