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Trial Steering Committee (TSC)

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The independent members of the TSC are: Dr Richard Haynes (Consultant Nephrologist; chair); Dr Nick Selby (Consultant Nephrologist); and Christopher Allison (Patient Representative).

Independent Data Monitoring Committee

The independent members of the DMC are: Dr John Firth (Consultant Nephrologist; chair); Dr Paul Kalra (Consultant Cardiologist); and Mrs Merryn Voysey (Statistician).

Birmingham Clinical Trial Unit

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Figure S1: Least Squares means plot (Sensitivity analysis (CKD-EPI equation 2009))

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Figure S2: Least Squares means plot (Sensitivity analysis (4-MDRD₁₈₆ equation))

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• eGFR values after commencing Kidney replacement therapy (i.e. dialysis/transplant) are not included in the analysis.

Figure S3: Least Squares means plot (Pattern Mixture Model (PMM) Flat value 5ml/min/1.73m² imputation - 4-MDRD₁₇₅ equation)



Note:

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Figure S4: Least Squares means plot (Pattern mixture Model (PMM) Flat value 5ml/min/1.73m² imputation – CKD-EPI equation 2009)



Note:

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Figure S5: Least Squares means plot (Pattern Mixture Model (PMM) Flat value 5ml/min/1.73m² imputation – 4-MDRD₁₈₆ equation)



Note:

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Figure S6: Least Squares means plot (Pattern Mixture Model (PMM) Flat value 7ml/min/1.73m² imputation - 4-MDRD₁₇₅ equation)

Note:

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Figure S8: Least Squares means plot (Pattern Mixture Model (PMM)L Flat value $7ml/min/1.73m^2$ imputation – 4-MDRD₁₈₆ equation)



Note:

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Figure S9: Least Squares means plot (Pattern Mixture Model (PMM) Last Observation Carried Forward (LOCF) imputation – 4-MDRD₁₇₅ equation)

Note:

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Figure S10: Least Squares means plot (Pattern mixture model of Last Observation Carried Forward imputation – CKD-EPI equation 2009)



Note:

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Figure S11: Least Squares means plot (Pattern mixture model Last Observation Carried Forward imputation – 4-MDRD₁₈₆ equation)



Note:

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Figure S12: Joint model plot of eGFR data (4-MDRD₁₇₅ equation)

*<u>Event</u>=participants that had a Kidney replacement therapy (i.e. dialysis or transplant) or reached ESKD. *Time scale is adjusted by taking away participant's survival time.*



Figure S13: Least Squares means plot - Joint model (4-MDRD₁₇₅ equation)

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Figure S14: Joint model plot of eGFR data (CKD-EPI equation 2009)

<u>Event</u>=participants that had a Kidney replacement therapy (i.e. dialysis or transplant) or reached ESKD. *Time scale is adjusted by taking away participant's survival time.*



Figure S15: Least Squares means plot - Joint model (CKD-EPI equation 2009)

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Figure S16: Joint model plot of eGFR data (4-MDRD₁₈₆ equation)

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*<u>Event</u>=participants that had a Kidney replacement therapy (i.e. dialysis or transplant) or reached ESKD. *Time scale is adjusted by taking away participant's survival time.*



Figure S17: Least Squares means plot - Joint model (4-MDRD₁₈₆ equation)

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			Mixed-effects			
	Time				linear regression	
	noint	Summary Statistic	STOP	Continue	Est. Mean Diff	
	point				(95% CI)*	
					P-value	
	3	Ν	187	190		
	months	Empirical Mean [SD]	16.9 [6.5]	16.9 [6]	-	
		LS-Mean \pm [SE]	$18.62 \pm [0.26]$	$18.58 \pm [0.29]$		
	6	Ν	166	172		
	months	Empirical Mean [SD]	16.3 [6.5]	16.6 [6.7]	-	
	monuis	LS-Mean \pm [SE]	$17.31 \pm [0.29]$	$18.02 \pm [0.33]$		
	9	Ν	148	157		
	months	Empirical Mean [SD]	16.2 [6.4]	16.7 [6.3]	-	
	monuis	LS-Mean \pm [SE]	$16.42 \pm [0.32]$	$17.25 \pm [0.31]$		
	12	Ν	130	142		
	months	Empirical Mean [SD]	16.1 [6.4]	16.4 [6.7]	-	
	montins	LS-Mean \pm [SE]	$15.78 \pm [0.36]$	$16.44 \pm [0.36]$		
	15	Ν	117	122		
	1J months	Empirical Mean [SD]	15.9 [6.4]	16 [6.3]	-	
	montins	LS-Mean \pm [SE]	$14.89 \pm [0.37]$	$15.89 \pm [0.38]$		
1 ²)	18	Ν	100	108		
/3n	months	Empirical Mean [SD]	16.3 [6.7]	17.2 [6.2]	-	
FR /1.7		LS-Mean \pm [SE]	$14.56 \pm [0.43]$	$15.69 \pm [0.40]$		
in/	21 months	Ν	96	99		
, L/n		Empirical Mean [SD]	16.1 [6.8]	16.8 [6.3]	-	
(m]		LS-Mean \pm [SE]	$14.08 \pm [0.48]$	$15.28 \pm [0.43]$		
•	24 months	Ν	88	95		
		Empirical Mean [SD]	15.7 [7.3]	16.3 [5.5]	-	
		LS-Mean \pm [SE]	$13.09 \pm [0.54]$	$14.16 \pm [0.40]$		
	27 months	Ν	78	87		
		Empirical Mean [SD]	15.6 [7.1]	15.5 [5.5]	-	
		LS-Mean \pm [SE]	$13.00 \pm [0.54]$	$13.45 \pm [0.50]$		
	30 months	Ν	69	80		
		Empirical Mean [SD]	15.7 [7.5]	15.7 [7]	-	
		LS-Mean \pm [SE]	$12.36 \pm [0.59]$	$13.42 \pm [0.63]$		
	33 months	Ν	59	66		
		Empirical Mean [SD]	15.7 [7.9]	15.9 [6.4]	-	
		LS-Mean \pm [SE]	$11.85 \pm [0.65]$	$13.05 \pm [0.55]$		
	36	Ν	56	69		
	30 months	Empirical Mean [SD]	16.4 [8.2]	16.1 [7.1]		
		LS-Mean \pm [SE]	$12.04 \pm [0.69]$	$12.79 \pm [0.61]$	-0.75 (-2.53, 1.02)	

 Table S1: Sensitivity analysis (CKD-EPI equation 2009)

*Adjusted for minimisation variables (age, eGFR, proteinuria, MAP, diabetes), time-point and treatment by time interaction. A compound symmetry covariance structure is assumed in the model and robust standard errors used. Continue group used as reference category in the model and values >0 indicate better outcome for STOP group. LS-Mean=Least squares mean; SE=Standard Error

<u>Note</u>: eGFR values after commencing Kidney replacement therapy (i.e. dialysis/transplant) are not included in the analysis. Confidence interval widths have not been adjusted for multiplicity and may not be used in place of hypothesis testing.

					Mixed-effects linear regression	
	Time point	Summary Statistic	STOP	Continue	Est. Mean Diff (95% CI)* P-value	
	3 months	Ν	187	190		
		Empirical Mean [SD]	16.9 [6.5]	16.9 [6]	-	
		LS-Mean ± [SE]	$20.02 \pm [0.27]$	$19.94 \pm [0.30]$		
	6		166	1/2		
	months	Empirical Mean [SD] 16.3 [6.5] 16.6 [6.7] 10.50 10.50 10.50 10.50		-		
		LS-Mean \pm [SE]	$18.68 \pm [0.30]$	$19.38 \pm [0.35]$		
	9		148	157		
	months	Empirical Mean [SD]	10.2[0.4]	10.7[0.3]	-	
		LS -Mean $\pm [SE]$	$1/./0 \pm [0.33]$	$18.01 \pm [0.33]$		
	12	IN Empirical Maan [SD]	150	142 164[67]		
	months	$\frac{\text{Empirical Wealt}[SD]}{\text{I S Moon} + [SE]}$	10.1 [0.4] $17 13 \pm [0.37]$	10.4 [0.7] $17.77 \pm [0.38]$	-	
		1000000000000000000000000000000000000	$17.13 \pm [0.37]$ 117	$17.77 \pm [0.36]$ 122		
	15 months	Fmnirical Mean [SD]	159[67]	16 [6 3]	_	
		I S-Mean + [SF]	16.23 + [0.39]	10[0.3] 1724 + [040]	-	
	18 months	N	10.25 ± [0.57]	108		
3m)		Empirical Mean [SD]	163[67]	17 2 [6 2]	_	
GFR in/1.73		LS-Mean + [SE]	15.90 + [0.45]	17.06 + [0.42]		
	21 months	N	96	99		
e /m		Empirical Mean [SD]	16.1 [6.8]	16.8 [6.3]	-	
nL		LS-Mean \pm [SE]	$15.40 \pm [0.50]$	$16.65 \pm [0.45]$		
\smile	24 months	N	88	95		
		Empirical Mean [SD]	15.7 [7.3]	16.3 [5.5]	-	
		LS-Mean ± [SE]	$14.42 \pm [0.57]$	$15.52 \pm [0.42]$		
	27 months	Ν	78	87		
		Empirical Mean [SD]	15.6 [7.1]	15.5 [5.5]	-	
		LS-Mean ± [SE]	$14.31 \pm [0.56]$	$14.79 \pm [0.52]$		
	30 months	Ν	69	80		
		Empirical Mean [SD]	15.7 [7.5]	15.7 [7]	-	
	monuis	LS-Mean \pm [SE]	$13.64 \pm [0.62]$	$14.75 \pm [0.66]$		
	33 months	N	59	66		
		Empirical Mean [SD]	15.7 [7.9]	15.9 [6.4]	-	
		LS-Mean \pm [SE]	$13.14 \pm [0.68]$	$14.41 \pm [0.57]$		
	36	Ν	56	69		
	months	Empirical Mean [SD]	16.4 [8.2]	16.1 [7.1]		
		LS-Mean \pm [SE]	$13.35 \pm [0.72]$	$14.12 \pm [0.64]$	-0.77 (-2.63, 1.10)	

 Table S2: Sensitivity analysis (4-MDRD₁₈₆ equation)

*Adjusted for minimisation variables (age, eGFR, proteinuria, MAP, diabetes), time-point and treatment by time interaction. A compound symmetry covariance structure is assumed in the model and robust standard errors used. Continue group used as reference category in the model and values >0 indicate better outcome for STOP group. LS-Mean=Least squares mean; SE=Standard Error

<u>Note</u>: eGFR values after commencing Kidney replacement therapy (i.e. dialysis/transplant) are not included in the analysis. And Confidence interval widths have not been adjusted for multiplicity and may not be used in place of hypothesis testing.

Pattern Mixture Model	eGFR Equation	Imputation	Summary Statistic	STOP	Continue	Mixed-effects linear regression Estimated Mean Diff (95% CI)* At 3 years
		Flat value		9.38 ±	9.91 ±	-0.54 (-1.72,
		5ml/min		[0.43]	[0.42]	0.65)
	MDRD ₁₇₅	Flat value		$10.56 \pm$	$10.99 \pm$	-0.43 (-1.53,
	11121021/5	7ml/min		[0.41]	[0.38]	0.66)
		LOCF		$12.11 \pm$	$12.52 \pm$	-0.41 (-1.45,
				[0.38]	[0.37]	0.63)
n ²)	CKD-EPI	Flat value		9.19 ±	9.63 ±	-0.43 (-1.61,
/3n		5ml/min	LS-Mean \pm	[0.43]	[0.41]	0.75)
HR		Flat value		$10.37 \pm$	$10.70 \pm$	-0.33 (-1.42,
G úl		7ml/min		[0.41]	[0.38]	0.76)
e u/u		LOCE	years	$11.77 \pm$	$12.15 \pm$	-0.38 (-1.43,
lm)		LUCF		[0.39]	[0.37]	0.68)
	MDRD ₁₈₆	Flat value		$9.78 \pm$	$10.37 \pm$	-0.59 (-1.87,
		5ml/min		[0.47]	[0.45]	0.69)
		Flat value		$10.96 \pm$	$11.44 \pm$	-0.48 (-1.67,
		7ml/min		[0.44]	[0.41]	0.70)
		LOCE		$12.84 \pm$	$13.28 \pm$	-0.44 (-1.54,
		LUCF		[0.41]	[0.39]	0.66)

Table S3: Pattern Mixture Model results at 3 years' time-point

*Adjusted for minimisation variables (age, eGFR, proteinuria, Mean Arterial Pressure, diabetes), time-point and treatment by time interaction. A compound symmetry covariance structure is assumed in the model and robust standard errors used. Continue group used as reference category in the model and values >0 indicate better outcomes for STOP group.

LOCF=Last observation carried forward; LS-Mean=Least squares mean; SE=Standard Error Note:

 Table S4: Joint Model results at 3 years' time-point

		Summary Statistic			Joint model	
Joint Model	eGFR Equation		STOP	Continue	Estimated Mean Diff (95% CI)* At 3 years	Hazard Ratio (95% CI) ^{\$}
eGFR (mL/min/1.73m ²)	MDRD ₁₇₅	LS-Mean ± [SE] at 3	$12.17 \pm$	$12.99 \pm$	-0.82 (-2.01,	1.41 (0.93,
	175		[0.45]	[0.42]	0.37)	2.12)
	CKD-EPI		$11.63 \pm$	$12.49 \pm$	-0.85 (-2.07,	1.40 (0.93,
			[0.46]	[0.43]	0.36)	2.10)
	MDRD ₁₈₆	years	$12.93 \pm$	$13.80 \pm$	-0.87 (-2.13,	1.41 (0.93,
			[0.48]	[0.44]	0.39)	2.12)

*Adjusted for minimisation variables (age, eGFR, proteinuria, Mean Arterial Pressure, diabetes), time-point and treatment by time interaction. A compound symmetry covariance structure is assumed in the model and robust standard errors used. Continue group used as reference category in the model and values >0 indicate better outcomes for STOP group.

\$-Adjusted for minimisation variables (age, eGFR, proteinuria, MAP, diabetes).

LOCF=Last observation carried forward; LS-Mean=Least squares mean; SE=Standard Error Note: