STOP-ACEi

CRF04 - 3-MONTHLY VISITS

One form to be completed for each 3-monthly trial visit.

Name of person that completed CRF, please print: This person must be listed on the STOP-ACEi delegation log.	……
Date CRF completed:	D D / M M M / Y Y Y Y

Part A: Identifying Details

Trial No.:	Centre: ……
DOB: M M M / Y Y Y Y	Assessment date: D D / M M M / Y Y Y Y

Part B: Assessment point

☐ Visit 2 (month 3)	☐ Visit 3 (month 6)	☐ Visit 4 (month 9)	☐ *Visit 5 (month 12)
☐ Visit 6 (month 15)	☐ Visit 7 (month 18)	☐ Visit 8 (month 21)	☐ *Visit 9 (month 24)
☐ Visit 10 (month 27)	☐ Visit 11 (month 30)	☐ Visit 12 (month 33)	☐ *Visit 13 (month 36)

*For months 12, 24 and 36, please arrange for the participant to complete the KDQOL-SF™ questionnaire. All additional yearly assessments in this CRF are required for months 12, 24 and 36.

Part C: Continued trial participation

Death

Has the participant died since the last trial visit? If yes, please provide details. No ☐ Yes ☐

Date of death: D D / M M M / Y Y Y Y

Cause of death category: ☐ 1 – Cancer, 2 – Cardiovascular, 3 – Cerebrovascular, 4 – Renal, 5 – Hepatic, 6 – Respiratory, 7 – Neurodegenerative, 8 – Accidental (death not caused by disease), 9 – Other

Details: ……

If the participant has died, please also complete CRF 10: SAE form and report this to the trial office within 24 hours of notification.

Withdrawal

Is the participant willing to continue in the study? No ☐ Yes ☐

Has the participant withdrawn from the study? If yes, please provide details. No ☐ Yes ☐

Reason:
- ☐ Participant lost to follow-up
- ☐ Participant withdrew consent, reason if given: ……
- ☐ Clinical decision. Details: ……
- ☐ Other. Details: ……

Type of withdrawal: (Select all that apply)

Withdrawal from trial treatment	No ☐	Yes ☐
Withdrawal from trial follow-up schedule	No ☐	Yes ☐
Withdrawal of optional consent – trial samples	No ☐	Yes ☐
Withdrawal of optional consent – access to HSCIC data	No ☐	Yes ☐
Withdrawal of consent to use patient records for trial follow-up	No ☐	Yes ☐
Withdrawal of consent to use existing anonymised samples	No ☐	Yes ☐

Other. Details: ……

Part D: Basic assessments

Weight (only to be performed at the baseline visit and at months 12, 24 and 36)	
Weight: ☐☐☐.☐ kg, to nearest 0.1 kg	NB. The database will calculate BMI using height recorded at the baseline visit and weight reported here.
Blood pressure	
Blood pressure: ☐☐☐ / ☐☐☐ mmHg	NB. Blood pressure should be measured according to current BHS guidelines.

Part E: Lab assessments (All assessments should be performed at site according to normal local practice)

eGFR	
eGFR will be calculated by the trial database system according to the 4V-MDRD equation. Only the creatinine level is required here, but please calculate eGFR for clinical monitoring.	
Serum creatinine: ☐☐☐☐ µmol/L	
Biochemical profile	
Sodium: ☐☐☐ mmol/L	Alkaline phosphatase: ☐☐☐ U/L
Potassium: ☐☐.☐ mmol/L	Albumin: ☐☐ g/L
Bicarbonate: ☐☐.☐ mmol/L	Total protein: ☐☐ g/L
Calcium: ☐.☐☐ mmol/L	Alanine transferase: ☐☐ U/L
Phosphate: ☐.☐☐ mmol/L	
Full blood count	
Haemoglobin: ☐☐☐ g/L	Platelets: ☐☐☐ $x10^9$/L
Urinary protein:creatinine ratio (PCR) or albumin:creatinine ratio (ACR) by early morning spot urine	
Urinary PCR: ☐☐☐☐ mg/mmol	Urinary ACR: ☐☐☐☐.☐ mg/mmol
C-reactive Protein (CRP; only to be performed at the baseline visit and at months 12, 24 and 36)	
CRP: ☐☐☐.☐ mg/L	

Part F: Sample tracking (only to be performed at the baseline visit and at months 12, 24 and 36)

Tracking for centrally analysed samples. Approximately 1 mL is required for each aliquot.

Sample type	Was the sample taken?		Was sample taken on date of assessment?		Date sample taken If different to assessment date
	No	Yes	No	Yes	
Standard trial sample, serum All trial participants. 2 x aliquots required.	☐	☐	☐	☐	DD/MM/YYYY
Standard trial sample, EDTA plasma All trial participants. 2 x aliquots required.	☐	☐	☐	☐	DD/MM/YYYY
Biomarker sample, serum Only for participants that have provided optional consent. 3 x aliquots required.	☐	☐	☐	☐	DD/MM/YYYY
Biomarker sample, urine Only for participants that have provided optional consent. 3 x aliquots required.	☐	☐	☐	☐	DD/MM/YYYY

Problems with sample preparation
Please note any problems with sample preparation here. E.g. samples left out overnight, not enough serum collected etc.

Part G: Six-Minute Walk-Test (only to be performed at the baseline visit and at months 12, 24 and 36)

Six-minute walk test (only to be performed at the baseline visit and at months 12, 24 and 36)		
Did the participant undergo the 6-minute walk test?	No ☐	Yes ☐
If no, reason not performed: (Please select one option)	Clinical reason ☐	Other reason ☐
	Details: ……	
Total distance covered in 6 minutes: ☐☐☐ m rounded to the nearest metre		
Was the test stopped prematurely?	No ☐	Yes ☐
If yes, stopped because of: (Please select one option)	Breathlessness ☐	Chest pain ☐
	Fatigue ☐	Other pain (e.g. joint) ☐
	Claudication ☐	
	Other ☐, specify: ……	

Part H: Clinical visits

Clinical visits		
Has the participant been seen by a doctor, nurse or other healthcare professional in primary care since the last trial visit?	No ☐	Yes ☐
Has the participant been seen in a hospital outpatients department since the last trial visit?	No ☐	Yes ☐
Has the participant been seen in a hospital A&E department since the last trial visit?	No ☐	Yes ☐
If yes, please record any related AEs or changes to medications in the AE and Medications sections of this form.		
Hospital admissions		
Has the participant been admitted to hospital since the last trial visit?	No ☐	Yes ☐
If yes, please provide the details below and record the details of any related AEs or changes to medications in the AE and Medications sections of this form. For additional hospital admissions, please use CRF05: Additional Hospital Admissions.		
Date admitted:	DD/MMM/YYYY	
Have they been discharged? No ☐ Yes ☐ - If yes, date:	DD/MMM/YYYY	
Was the visit related to the participant's CKD?	No ☐	Yes ☐
Main reason for admission: ……		
Treatment given:	Prescription medicine** ☐	Advice to buy OTC medication** ☐
	Advice ☐	Referral to a specialist ☐
	Other ☐, specify: ……	

** Please note any new medications or changes to existing medications in the medications section of this form.

If any clinical visit relates to a serious adverse event, please also report it within 24 hours of notification using CRF10: SAE form.

Part I: Adverse events

CKD progression				
Since the last trial visit, has the participant…?	**No**	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Started renal replacement therapy	☐	☐	……/……/……	……
Had a diagnosis of ESRD	☐	☐	……/……/……	……

Cardiovascular events

Has the participant had any of the following major cardiovascular events since the last trial visit?

Event code	Event	No	Yes
1	Hospitalisation for heart failure	☐	☐
2	STEMI / MI	☐	☐
3	NSTEMI	☐	☐
4	Stroke / CVE	☐	☐

If the participant had any of the above major cardiovascular events. Please enter the dates for all events since the last trial visit below. E.g. if the participant was admitted for heart failure twice since the last visit, give dates for both events. If you need more space, please use another CRF04.

Event code	Date	Event Code	Date
	D D / M M M / Y Y Y Y		D D / M M M / Y Y Y Y
	D D / M M M / Y Y Y Y		D D / M M M / Y Y Y Y
	D D / M M M / Y Y Y Y		D D / M M M / Y Y Y Y
	D D / M M M / Y Y Y Y		D D / M M M / Y Y Y Y

Heart Failure

In the responsible clinician's opinion, does the patient have heart failure? If yes, please provide further information below. No ☐ Yes ☐

Date of diagnosis: D D / M M M / Y Y Y Y Please only enter the date for the first diagnosis of heart failure.

Current NYHA Functional Classification (please select one):

- ☐ Class 1: Patients with no limitation of activities, they suffer no symptoms from ordinary activities.
- ☐ Class 2: Patients with slight, mild limitation of activity; they are comfortable with rest or with mild exertion.
- ☐ Class 3: Patients with marked limitation of activity; they are comfortable only at rest.
- ☐ Class 4: Patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest.

Please indicate which major Framingham criteria are met: NK= not known.

	No	Yes	NK
Paroxysmal nocturnal dyspnoea	☐	☐	☐
Neck vein distention	☐	☐	☐
Rales	☐	☐	☐
Radiographic cardiomegaly	☐	☐	☐
Acute pulmonary oedema	☐	☐	☐
S3 gallop	☐	☐	☐
Increased central venous pressure (>16 cm H_2O at right atrium)	☐	☐	☐
Hepatojugular reflux	☐	☐	☐
Weight loss >4.5 kg in 5 days in response to treatment	☐	☐	☐

…Heart Failure cont'd

Please indicate which minor Framingham criteria are met: NK= not known.

Bilateral ankle oedema	No ☐	Yes ☐	NK ☐
Nocturnal cough	No ☐	Yes ☐	NK ☐
Dyspnoea on ordinary exertion	No ☐	Yes ☐	NK ☐
Hepatomegaly	No ☐	Yes ☐	NK ☐
Pleural effusion	No ☐	Yes ☐	NK ☐
Decrease in vital capacity by one third from maximum recorded	No ☐	Yes ☐	NK ☐
Tachycardia (heart rate >120 beats/min.)	No ☐	Yes ☐	NK ☐

Since the last trial visit…

…Was diuretic started or dose of diuretic increased for heart failure?	No ☐	Yes ☐	NK ☐
…Has a BNP (brain natriuretic peptide) measure been taken?	No ☐	Yes ☐	NK ☐
…Has an echo been performed? If yes, please also complete the echo section.	No ☐	Yes ☐	NK ☐
Is there another plausible cause of symptoms? E.g. fluid overload	No ☐	Yes ☐	NK ☐

Adverse Events – Please indicate all new events or diagnoses the participant has had since the last trial visit

If there have been multiple events, please record the date of the first event since the last trial visit. Please use the 'details' section to give further information (e.g. if there are multiple events). If only the month is known, please input as the 1st of that month.

Other Cardiovascular Disease	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Angina	☐	☐	……/……/……	……
Coronary Intervention (PCI)	☐	☐	……/……/……	……
Coronary Intervention (CABG)	☐	☐	……/……/……	……
Carotid intervention	☐	☐	……/……/……	……
Hypertension	☐	☐	……/……/……	……
Atrial fibrillation / flutter	☐	☐	……/……/……	……
Venous thromboembolism	☐	☐	……/……/……	……
Peripheral vascular disease	☐	☐	……/……/……	……
If yes, please indicate which:	Claudication			No ☐ Yes ☐
	Radiological/surgical intervention			No ☐ Yes ☐
	Amputation			No ☐ Yes ☐
	Other, specify: ……			No ☐ Yes ☐
Other cardiovascular condition	☐	☐	……/……/……	……

Diabetes	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Type 1 diabetes mellitus	☐	☐	……/……/……	……
Type 2 diabetes mellitus	☐	☐	……/……/……	……

Adverse Events – Please indicate all new events or diagnoses the participant has had since the last trial visit

Malignancy	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Any malignancy	☐	☐	...../...../.....	.....
If yes, please indicate which:	Solid organ		No ☐ Yes ☐	
	Skin – non-melanoma		No ☐ Yes ☐	
	Haematological		No ☐ Yes ☐	
	Other, specify:		No ☐ Yes ☐	
Gastrointestinal	No ☐ Yes ☐ – if yes, please provide details			
Please only record GI symptoms that the responsible clinician considers significant				
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Bloating, abdominal distention or abdominal pain	☐	☐	...../...../.....	.....
Constipation	☐	☐	...../...../.....	.....
Dyspepsia	☐	☐	...../...../.....	.....
Gastritis	☐	☐	...../...../.....	.....
Loose stools / diarrhoea	☐	☐	...../...../.....	.....
Nausea / vomiting	☐	☐	...../...../.....	.....
Ulceration	☐	☐	...../...../.....	.....
Other GI condition	☐	☐	...../...../.....	.....
Musculoskeletal or connective tissue disorders	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Avascular osteonecrosis	☐	☐	...../...../.....	.....
Fractures	☐	☐	...../...../.....	.....
Osteoporosis	☐	☐	...../...../.....	.....
Osteopenia	☐	☐	...../...../.....	.....
Other musculoskeletal or connective tissue disorder	☐	☐	...../...../.....	.....
Infection	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Urinary tract infection	☐	☐	...../...../.....	.....
Cytomegalovirus	☐	☐	...../...../.....	.....
Herpes Simplex Virus	☐	☐	...../...../.....	.....
Varicella Zoster Virus	☐	☐	...../...../.....	.....
Human Immunodeficiency Virus	☐	☐	...../...../.....	.....
Hepatitis B	☐	☐	...../...../.....	.....

…Adverse events cont'd – Please indicate all new events or diagnoses the participant has had since the last trial visit

… Infection cont'd	**No**	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Hepatitis C	☐	☐	……/……/……	……
Other infection	☐	☐	……/……/……	……

Pulmonary disease	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
COPD	☐	☐	……/……/……	……
Interstitial lung disease	☐	☐	……/……/……	……
Other pulmonary disease	☐	☐	……/……/……	……

Other	No ☐ Yes ☐ – if yes, please provide details			
	No	**Yes**	**Date** (dd/mmm/yyyy)	**Details**
Current pregnancy	☐	☐	……/……/……	……
Psychosis	☐	☐	……/……/……	……
Gout	☐	☐	……/……/……	……
Breathlessness	☐	☐	……/……/……	……
Peripheral Oedema	☐	☐	……/……/……	……
Anaemia	☐	☐	……/……/……	……
Leukopenia	☐	☐	……/……/……	……
Thrombocytopenia	☐	☐	……/……/……	……
Endocrine or metabolic disorder	☐	☐	……/……/……	……
Cataracts	☐	☐	……/……/……	……
Other, please specify	☐	☐	……/……/……	……
Other, please specify	☐	☐	……/……/……	……
Other, please specify	☐	☐	……/……/……	……
Other, please specify	☐	☐	……/……/……	……

SAE check

Since the last trial visit, has the participant experienced any adverse events that:

Resulted in death	No ☐	Yes ☐
Were life threatening	No ☐	Yes ☐
Required in-patient hospitalisation or prolongation of existing hospitalisation	No ☐	Yes ☐
Resulted in persistent or significant disability or incapacity	No ☐	Yes ☐
Resulted in a congenital anomaly or a birth defect	No ☐	Yes ☐

If you have answered 'yes' to any of the SAE check questions above, please complete an SAE form and alert the STOP-ACEi Trial Office within 24 hours of being notified of the event.

Part J: Medications

ESA dose

Is the participant currently on ESA treatment? No ☐ Yes ☐
If yes, please provide details here:

Type	No	Yes	Please see list of possible options at end of this document. Current dose	Unit	Current freq.	Route
Epoetin alfa (e.g. eprex)	☐	☐				
Epoetin beta (NeoRecormon®)	☐	☐				
Darbepoetin alfa (Aranesp®)	☐	☐				
Mircera	☐	☐				
Other, specify:	☐	☐				

Antihypertensive medications

Please indicate what antihypertensive medications the participant is currently taking.

Category	No	Yes	Type/brand name	Please see list of possible options at end of this document. Current dose	Unit	Current freq.	Route
ACE inhibitor	☐	☐					
ARB	☐	☐					
CCB	☐	☐					
Loop diuretic	☐	☐					
Thiazide diuretic	☐	☐					
Thiazide-like diuretic	☐	☐					
K^+-sparing diuretic	☐	☐					
Mineralocorticoid Receptor Antagonist e.g. spironolactone	☐	☐					
Alpha blocker	☐	☐					
Beta blocker	☐	☐					
Methyldopa	☐	☐					
Moxonidine	☐	☐					
Hydralazine	☐	☐					
Other antihypertensive	☐	☐					

Other concomitant medications

Is the participant currently taking any other medications? No ☐ Yes ☐
If yes, indicate what other medications the participant is currently taking:

Category	No	Yes	Category	No	Yes	Category	No	Yes
Statin	☐	☐	Clopidogrel	☐	☐	Mycophenolate mofetil (MMF)	☐	☐
Digoxin	☐	☐	Warfarin	☐	☐	Ciclosporin	☐	☐
Nitrate	☐	☐	Phosphate binders	☐	☐	Cyclophosphamide	☐	☐

…Other concomitant medications cont'd

Category	No	Yes	Category	No	Yes	Category	No	Yes
Fibrate	☐	☐	Calcium/Vitamin D	☐	☐	Azathioprine	☐	☐
Ezetimibe	☐	☐	Bisphosphonate	☐	☐	Tacrolimus	☐	☐
Aspirin	☐	☐	Prednisolone	☐	☐	Methotrexate	☐	☐
Bicarbonate	☐	☐	Metformin	☐	☐	NSAIDS	☐	☐
Sulphonylurea, e.g. glicazide	☐	☐	Sirolimus	☐	☐	Thiazolidinedione/glitazone	☐	☐
GLP-1 analogues/agonists, e.g. liraglutide, exenatide	☐	☐	SGLT2 inhibitor, e.g. dapagliflozin	☐	☐	DPP-4 inhibitor (incretins), e.g. sitagliptin, vildagliptin	☐	☐

Please detail any other medications the participant is currently taking. Only name/type is required.

Part K: Compliance

Compliance with trial treatment allocation

Has the participant remained compliant to their trial treatment allocation since the last trial visit? No ☐ Yes ☐

i.e. if on the experimental (discontinue ACEi/ARB) arm, hasn't taken any ACEis or ARBs
OR, if on the control (continue ACEi/ARB) arm, has continued to take their ACEis or ARBs.

If there has been non-compliance, please indicate the reasons (select all that apply):

Worsening renal function	No ☐	Yes ☐	Acute kidney injury	No ☐	Yes ☐
Hypertension	No ☐	Yes ☐	Hypotension	No ☐	Yes ☐
Hyperkalaemia	No ☐	Yes ☐	Hypokalaemia	No ☐	Yes ☐
Headache	No ☐	Yes ☐	Nausea/GI symptoms	No ☐	Yes ☐
Facial swelling / lip swelling	No ☐	Yes ☐	Dry cough	No ☐	Yes ☐
Dizziness	No ☐	Yes ☐	Angioedema	No ☐	Yes ☐
Rash	No ☐	Yes ☐	Taste disturbance	No ☐	Yes ☐

Other clinical reason No ☐ Yes ☐ – if yes, details: ……

Other reason No ☐ Yes ☐ – if yes, details: ……

If non-compliance relates to an AE, please also record this in the AEs section of this form.

Part L: 12-Lead ECG (only to be performed at the baseline visit and at months 12, 24 and 36)

12-lead ECG (only to be performed at the baseline visit and at months 12, 24 and 36)

Was a 12-lead ECG performed? No ☐ Yes ☐

If no, reason not done: ……

Ventricular rate: ☐☐☐ b.p.m. QTc duration: ☐☐☐ ms

The ECG is: (Please select one option) Normal ☐ Abnormal, not clinically significant ☐ Abnormal + clinically significant ☐

…12-lead ECG cont'd				
If abnormal and clinically significant, please provide details below (NK = not known).				
In the responsible clinician's opinion, is the ECG different to baseline?		No ☐	Yes ☐	NK ☐
If yes, please specify: ……				
Is there evidence of myocardial infarction?		No ☐	Yes ☐	NK ☐
Cardiac rhythm:	Sinus rhythm?	No ☐	Yes ☐	NK ☐
	Is there evidence of atrial fibrillation?	No ☐	Yes ☐	NK ☐
	Is there evidence of other supraventricular tachycardia? (e.g. flutter)	No ☐	Yes ☐	NK ☐
	Paced rhythm?	No ☐	Yes ☐	NK ☐
	Other rhythm abnormality, specify: ……			
Is there evidence of a conduction defect?		No ☐	Yes ☐	NK ☐
Is this left bundle branch block?		No ☐	Yes ☐	NK ☐
Other conduction defect, specify: ……				
Is there evidence of left ventricular hypertrophy?		No ☐	Yes ☐	NK ☐

Part M: Echocardiogram

Echocardiogram				
Has the participant had a cardiac echocardiogram since the last trial visit? If yes, please provide the available details for the most recent echo. Please record values that have not been indexed to body size. This is the most common measure available. NK = not known.		No ☐	Yes ☐	
Date of echo: D D / M M M / Y Y Y Y				
Is LV (left ventricular) ejection fraction known?		No ☐	Yes ☐ – If yes, please provide: ☐☐ %	
If a value for LVEF is not known, please indicate LV systolic function (please select one option):				
Normal ☐	Mildly impaired ☐	Moderately impaired ☐	Mod.-severely impaired ☐	Severely impaired ☐
Is estimated pulmonary artery systolic pressure known?		No ☐	Yes ☐ – If yes, please provide: ☐☐☐ mmHg	
Is left atrial volume known?		No ☐	Yes ☐ – If yes, please provide: ☐☐ mL^3	
Is there evidence of LV hypertrophy?		No ☐	Yes ☐ NK ☐	
If yes, severity (please select one option):		Mild ☐	Moderate ☐	Severe ☐ NK ☐

Part N: Visit checklist

In addition to the data above, the following forms may also be required for the 3-monthly visits:

- A copy of the completed KDQOL-SF™ form (for baseline (visit 1) and months 12, 24 and 36 only).
- CRF10: SAE form (where applicable).
- CRF05: Additional Hospital Admissions (where required).

Additional forms		
Has the KDQOL-SF ™ form been completed?	☐ No	☐ Yes

Thank you for completing the STOP-ACEi CRF04: 3-Monthly Visits

Please enter data online at: https://www.trials.bham.ac.uk/STOPACEi

STOP-ACEi Study Office, Birmingham Clinical Trials Unit, College of Medical & Dental Sciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT.
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STOP-ACEi website: www.birmingham.ac.uk/STOPACEi

Answer Options for Concomitant Medications

Unit		**Route**	**Frequency**
mg	Milligram	Intraarterial	Twice a day
mcg	Microgram	Intraperitoneal	Three times a day
g	Gram	Intravenous	Four times a day
Puffs		Oral	Hourly
U	Units	Respiratory (inhalation)	4 hourly
mL	Millilitre	Subcutaneous	Daily
mg/ml	Milligrams per millilitre	Topical	Alternate days
mg/kg	Milligrams per kilogram	Suppository	As desired
mcg/ml	Micrograms per millilitre	Intraocular	If necessary
AUC	Area Under Curve	Intramuscular	Slow release
Other, **specify**		Other, **specify**	Other, **specify**
Not known		Not known	Not known