Trial Management & Data Management

Launch Meeting

3rd April 2014, Lucas House, Birmingham

BIRMINGHAM CLINICAL TRIALS UNIT

UNIVERSITY OF BIRMINGHAM

Hull and East Yorkshire Hospitals NHS Trust

NHS

Trial coordination

Birmingham Clinical Trials Unit

- Trial coordination
- Data collection
- Data analysis
- Design and maintenance of the trial website and database
- Randomisation
- Safety reporting

Hull and East Yorkshire Hospitals NHS Trust

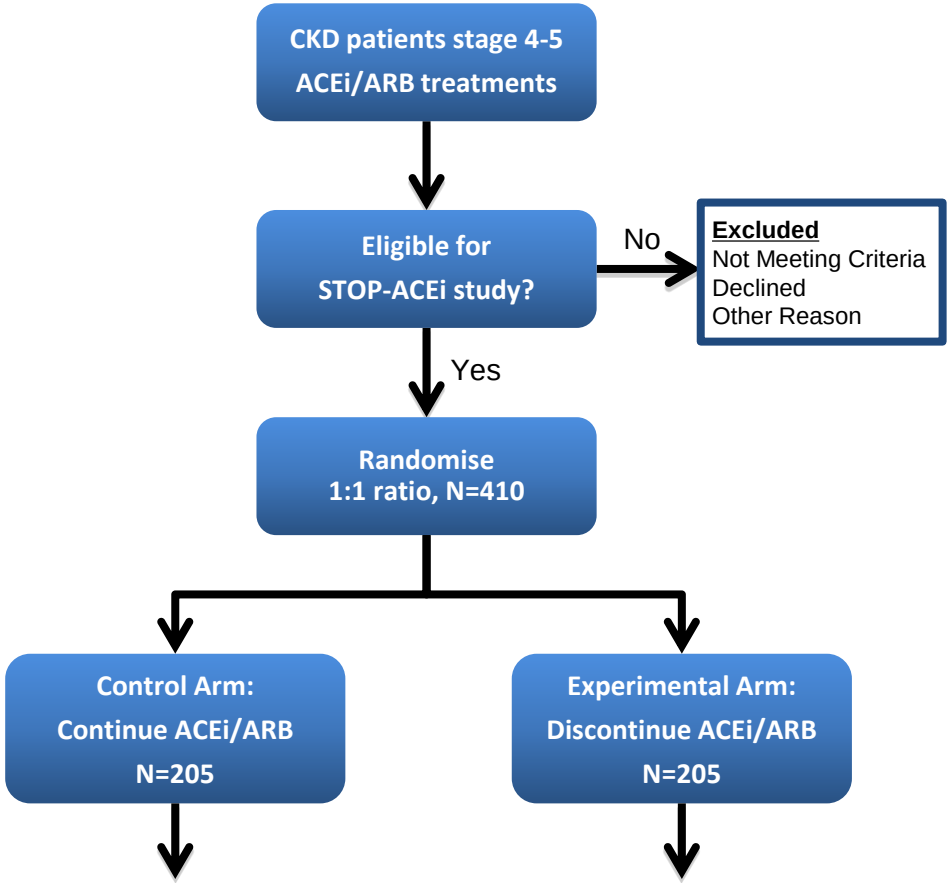
- Chief Investigator
- Sponsor
- Oversight
- Trial design
- Clinical lead

Hull and East Yorkshire Hospitals NHS Trust

Trial schema

2 years recruitment

3 years follow-up



3 Year Follow-Up

3-monthly visits	- routine tests (eGFR, FBC, BCP, urinary PCR), BP, documentation of ESA dose, adverse events, compliance and changes in medication
Extra tests at annual visits	- QOL questionnaire, weight and BMI, 6-minute walk test, ECG, and bloods for C-reactive protein, cystatin-C, NT-proBNP, ACE/renin levels and biomarkers

Patient Recruitment

Identify potential participants	
Against inclusion/exclusion criteria	From medical records

↓

Invite potential participants to take part	
1-2 weeks before next clinic appointment	REC-approved Letter to Accompany PIS
Record details of all participants considered for STOP-ACEi in the screening log	REC-approved Participant Information Sheet

↓

Discuss participation in STOP-ACEi	
At next clinic appointment	Discuss risks/benefits - equipoise

↓

Informed Consent Process	
Appropriately trained medically qualified staff	Optional consents

↓

Final eligibility check
Appropriately trained medically qualified staff

↓

RANDOMISE

Eligibility criteria

Inclusion criteria
Aged ≥18 years (male or female);
CKD stage 4 or 5 (eGFR <30mls/minute using the MDRD equation) and not on dialysis therapy;
Progressive deterioration in renal function (fall in eGFR of >2ml/min/year over previous 12-24 months) as measured by linear regression analysis.
Treatment with either an ACEi or ARB or a combination of both for >6 months with at least 25% of the maximum recommended daily dose on the day of consent;
Resting blood pressure (BP) ≤160/90 mmHg
At least 3 months of specialist renal follow-up at the time of entry into the trial;
Written, signed informed consent to the trial.

Eligibility criteria

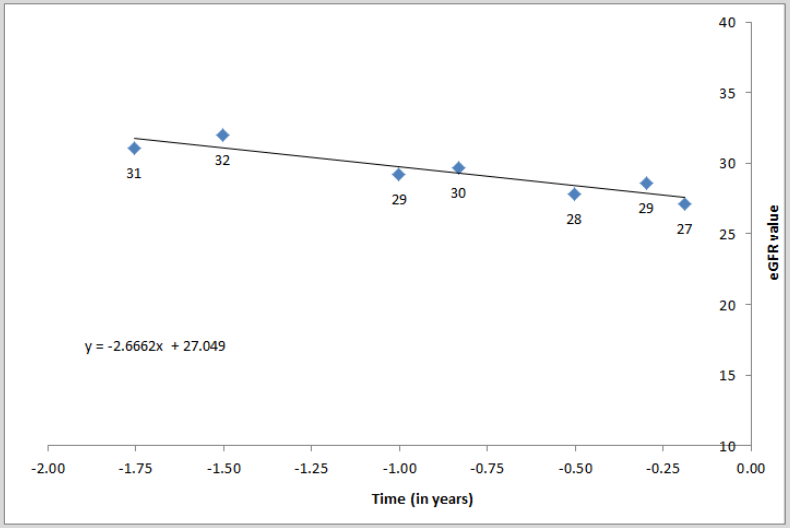
Exclusion criteria
Aged <18 years;
Uncontrolled hypertension (>160/90mmHg) or requirement for 5 or more agents to control BP;
Undergoing dialysis therapy;
Any condition which, in the opinion of the investigator, makes the participant unsuitable for trial entry due to prognosis/terminal illness with a projected survival of less than 12 months;
History of myocardial infarction or stroke in preceding 3 months;
Participation in an interventional research study in preceding 6 weeks;
Pregnancy, confirmed by positive pregnancy test, or breastfeeding;
Inability to provide informed consent (e.g. due to cognitive impairment);
Immune mediated renal disease requiring disease specific treatment;
Known drug or alcohol abuse;
Inability to comply with the trial schedule and follow-up.

Eligibility - eGFR decline

Progressive deterioration in renal function (fall in eGFR of >2ml/min/year over previous 12-24 months) as measured by linear regression analysis.

Male/Female	Male
Is ethnicity black?	No
Date of Birth:	01/01/1949
Screening date:	01/12/2013
Rate of decline:	-2.67 mL/min/year
Is patient eligible?	**ELIGIBLE**

Date of eGFR	Serum creatinine
01/03/2012	200
01/06/2012	195
01/12/2012	211
01/02/2013	208
01/06/2013	220
15/08/2013	215
23/09/2013	225



Screening log

STOP-ACEi Participant Screening Log

EudraCT number:	2013-003798-82	Investigator name:		Site name:	

Study title:	Multi-centre Randomised Controlled Trial of Angiotensin Converting Enzyme inhibitor (ACEi) / Angiotensin Receptor Blocker (ARB) withdrawal in advanced renal disease; The STOP-ACEi Trial

Please record details of all participants considered for potential participation in STOP-ACEi and reasons for non-participation, where available.

Codes

A. Recruited into STOP-ACEi	**G.** Patient declined because in other research
B. Not suitable because eGFR decline not >2mL/min/year	**H.** Patient declined because not interested in research/STOP-ACEi
C. Not suitable because blood pressure too high, or uncontrolled	**I.** Patient declined because visit assessments will take too long
D. Not suitable because history of MI/stroke in previous 3 months	**J.** Patient declined because concerned about trial intervention
E. Not suitable because not currently on ACEi/ARB treatment	**K.** Patient declined, but no reason given
F. Not suitable because didn't meet other eligibility criteria (please specify)	**L.** Other (please specify)

	Patient Initials	Patient DoB	Hospital Number	Date of screening (dd/mmm/yyyy)	Date sent PIS (dd/mmm/yyyy)	Recruited (yes/no)	Code/s see list on page 1	Further details	Study number (if recruited)
1.									
2.									
3.									

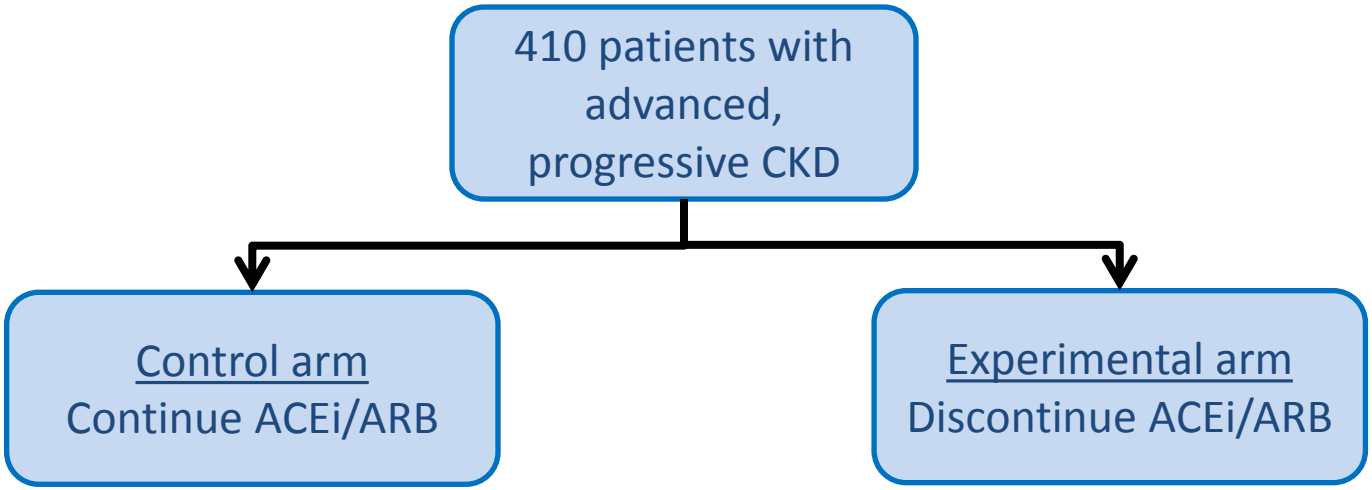
CONFIDENTIAL WHEN COMPLETED: PLEASE DELETE OR BLACK-OUT PATIENT INITIALS, DATE OF BIRTH AND HOSPITAL NUMBER BEFORE SENDING TO BCTU TO PREVENT SHARING OF PATIENT IDENTIFIABLE INFORMATION

Informed consent

- As per GCP
- By appropriately trained and medically qualified personnel
- Must be delegated

- After consent is obtained, can now randomise

Randomisation



What information is needed to randomise?

- Patient identifiers
- 3 x Serum creatinine to check eGFR decline
- eGFR to confirm stage 4 or 5
- BP to confirm controlled BP
- Eligibility check
- Who performed eligibility check
- Minimisation variables:

  Diabetes, BP, age, proteinuria, eGFR
- Confirmation of informed consent

Everything on CRF01 - Randomisation Notepad!

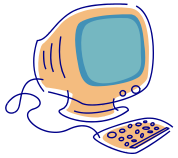
Randomisation

9am – 5pm, Mon-Fri
0800 953 0274

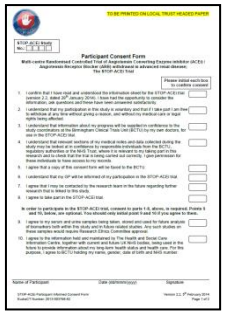
Collect info on
Rand. Notepad

Randomise

Confirmation
e-mail



24hrs / 7 days
www.trials.bham.ac.uk.stopacei



Complete trial
ID on ICF

Fax the completed
ICF to BCTU

0121 415 9135

BCTU will perform
checks

Common problems with ICFs

ICF not on headed paper

Trial ID not completed

Boxes ticked instead of initialled

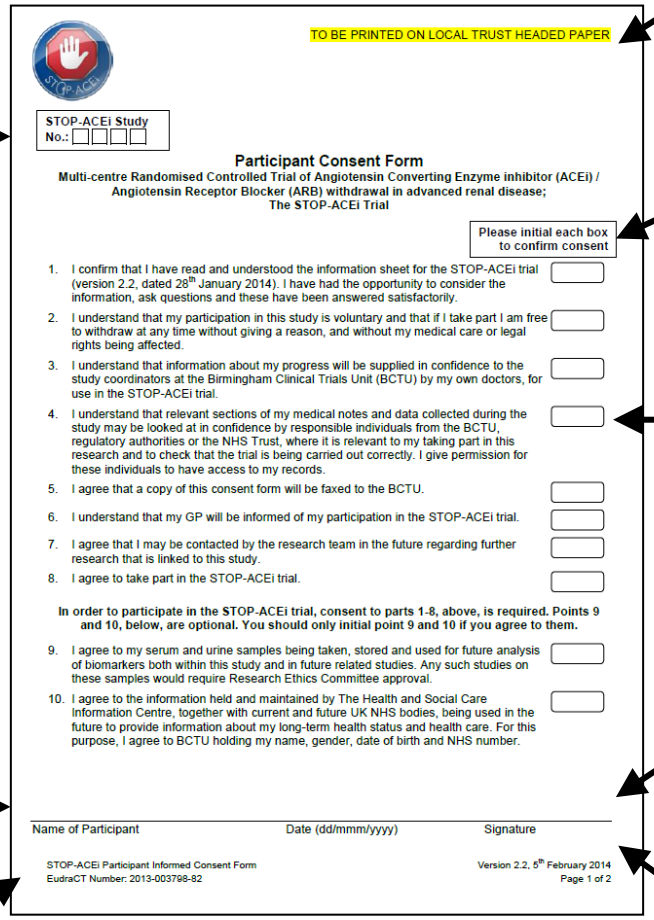
Some required boxes not initialled

Clinician counter-signing ICF not on del. log.

Missing signatures / dates

Incorrect version no.

Clinician counter-signing ICF on different date



TO BE PRINTED ON LOCAL TRUST HEADED PAPER

STOP-ACEi Study No.: ☐☐☐☐

Participant Consent Form

Multi-centre Randomised Controlled Trial of Angiotensin Converting Enzyme inhibitor (ACEi) / Angiotensin Receptor Blocker (ARB) withdrawal in advanced renal disease; The STOP-ACEi Trial

Please initial each box to confirm consent

1. I confirm that I have read and understood the information sheet for the STOP-ACEi trial (version 2.2, dated 28th January 2014). I have had the opportunity to consider the information, ask questions and these have been answered satisfactorily. ☐
2. I understand that my participation in this study is voluntary and that if I take part I am free to withdraw at any time without giving a reason, and without my medical care or legal rights being affected. ☐
3. I understand that information about my progress will be supplied in confidence to the study coordinators at the Birmingham Clinical Trials Unit (BCTU) by my own doctors, for use in the STOP-ACEi trial. ☐
4. I understand that relevant sections of my medical notes and data collected during the study may be looked at in confidence by responsible individuals from the BCTU, regulatory authorities or the NHS Trust, where it is relevant to my taking part in this research and to check that the trial is being carried out correctly. I give permission for these individuals to have access to my records. ☐
5. I agree that a copy of this consent form will be faxed to the BCTU. ☐
6. I understand that my GP will be informed of my participation in the STOP-ACEi trial. ☐
7. I agree that I may be contacted by the research team in the future regarding further research that is linked to this study. ☐
8. I agree to take part in the STOP-ACEi trial. ☐

In order to participate in the STOP-ACEi trial, consent to parts 1-8, above, is required. Points 9 and 10, below, are optional. You should only initial point 9 and 10 if you agree to them.

9. I agree to my serum and urine samples being taken, stored and used for future analysis of biomarkers both within this study and in future related studies. Any such studies on these samples would require Research Ethics Committee approval. ☐
10. I agree to the information held and maintained by The Health and Social Care Information Centre, together with current and future UK NHS bodies, being used in the future to provide information about my long-term health status and health care. For this purpose, I agree to BCTU holding my name, gender, date of birth and NHS number. ☐

Name of Participant | Date (dd/mmm/yyyy) | Signature

STOP-ACEi Participant Informed Consent Form
EudraCT Number: 2013-003798-82

Version 2.2, 5th February 2014
Page 1 of 2

Continued consent and withdrawal

- Consent an ongoing process
- Continued participation and consent recorded on visit CRFs
- Withdrawal
  - Withdrawn if consent is withdrawn
  - Not if a participant just stops taking study medication
  - Cause should be documented on the appropriate form e.g. consent withdrawn, lost to follow-up etc.

After randomisation

- Fax the participant's signed consent form to the STOP-ACEi trial office
- Give the participant a copy of the following documents:
  - Participant Advice Letter for treatment continuation/discontinuation
  - A blank copy of the participant diary – to be completed between visits and collected at each visit
  - A copy of the signed Consent Form
  - A copy of the Participant Information Sheet
- Send a copy of the GP letter for treatment continuation/discontinuation to the participant's GP
- File a copy of the Confirmation of Randomisation e-mail in the participant's case notes and a copy in the local Site File.
- File a copy of the Consent Form and Participant Information Sheet in the participant's case notes and file the original in the local Site File.
- Put the participant's details are listed with the Participant Trial Number in the Recruitment Log in the Site File.
- Perform baseline assessments

Participant Identification log

STOP-ACEi Participant Identification Log

EudraCT number:	2013-003798-82	Investigator name:		Site name:	

Study title:	Multi-centre Randomised Controlled Trial of Angiotensin Converting Enzyme inhibitor (ACEi) / Angiotensin Receptor Blocker (ARB) withdrawal in advanced renal disease; The STOP-ACEi Trial

Please record details of all participants that have been recruited onto the STOP-ACEi trial.

Trial Number	Participant Name	Participant DOB	Hospital Number	Date of Informed Consent (dd/mmm/yyyy)	Date of Randomisation if different (dd/mmm/yyyy)	Consented to giving biomarker samples? (yes/no)	Consented to giving access to central NHS data? (yes/no)

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Trial visits and procedures

- Screening, baseline and randomisation
- Telephone follow-up at 4-6 weeks post-randomisation
- 3-monthly follow-up visits for 3 years

Baseline	Informed consent	Randomisation	Demographics
	Medical history	CKD aetiology	Lifestyle indicators
	Baseline medications		
Telephone follow-up	Compliance	Medication changes	AEs
3-monthly visits	Blood pressure	eGFR	Biochemistry
	FBC	ESA dose	AEs
	Compliance	Medication changes	
Annual visits	QOL questionnaire	Weight & BMI	6-minute walk test
	ECG	CRP	Cystatin-C
	NT-proBNP	ACE/renin levels	Biomarker samples

Casenote documentation

- See guidelines in ISF
- When patient is approached
  - Name of trial
  - Date approached about study or PIS given
  - Copy of PIS
  - Date of consent + record of discussion to show patient is ‘informed’
  - Copy of signed consent form
  - Trial ID number
  - Arm they’ve been randomised to
  - Name of PI to contact about the study if any issues
- For each visit
  - Date and study visit number e.g. STOP-ACEi baseline visit
  - Any clinically relevant information e.g. medical history, changes to treatment/prescriptions, results of any medically relevant trial assessments
  - For AEs, a brief description of the event inc. start/stop dates and results of any clinically pertinent assessments made relating to the AE

QoL questionnaires

- Completed by participant
- Ideally alone to prevent influence
  - research nurse
  - family
- RN can check for completeness or causes for concern
- Should be done before randomisation on 1st visit
- Should be done before assessments on subsequent visits
- While patient is waiting to be seen

Trial samples

	What will be tested	Where analysed	When samples taken
Routine tests	Biochemical profile eGFR Full blood count Urinary PCR CRP	Locally, at your site.	Baseline Every 3-monthly trial visit (CRP taken annually)
Standard Trial Samples	Cystatin-C NT-proBNP ACE Renin levels	Centrally, at Hull lab	Baseline, Month 12, Month 24, Month 36
Optional Biomarker Samples	unknown biomarkers in future analysis	Centrally, at Hull lab	Baseline, Month 12, Month 36

- See protocol for details of BCP and FBC
- Centrally analysed samples
  - Prepare according to SOP in site file
  - Store at -80°C until sent to central lab in Hull
  - BCTU to arrange transport approx. annually

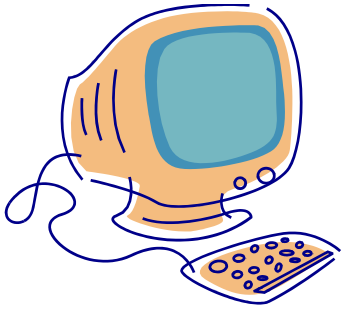
CRFs and data entry

- CRFs are in your site file or can be downloaded from the trial website
  - CRF01 – Randomisation Form
  - CRF02 – Baseline assessment
  - CRF03 – Telephone follow-up
  - CRF04 – 3-monthly visits
  - CRF05 – Additional clinical visits
  - CRF06 – Lab results – used by central lab staff
  - CRF10 – SAE form
- Participant diaries are there to help fill in the AE and clinic visit parts of the CRFs
- Don’t forget KDQOL-SF questionnaires

CRFs and data entry

- Completed paper CRFs can be submitted to BCTU by post or fax

- Can enter data directly into online system – will check for errors / omissions

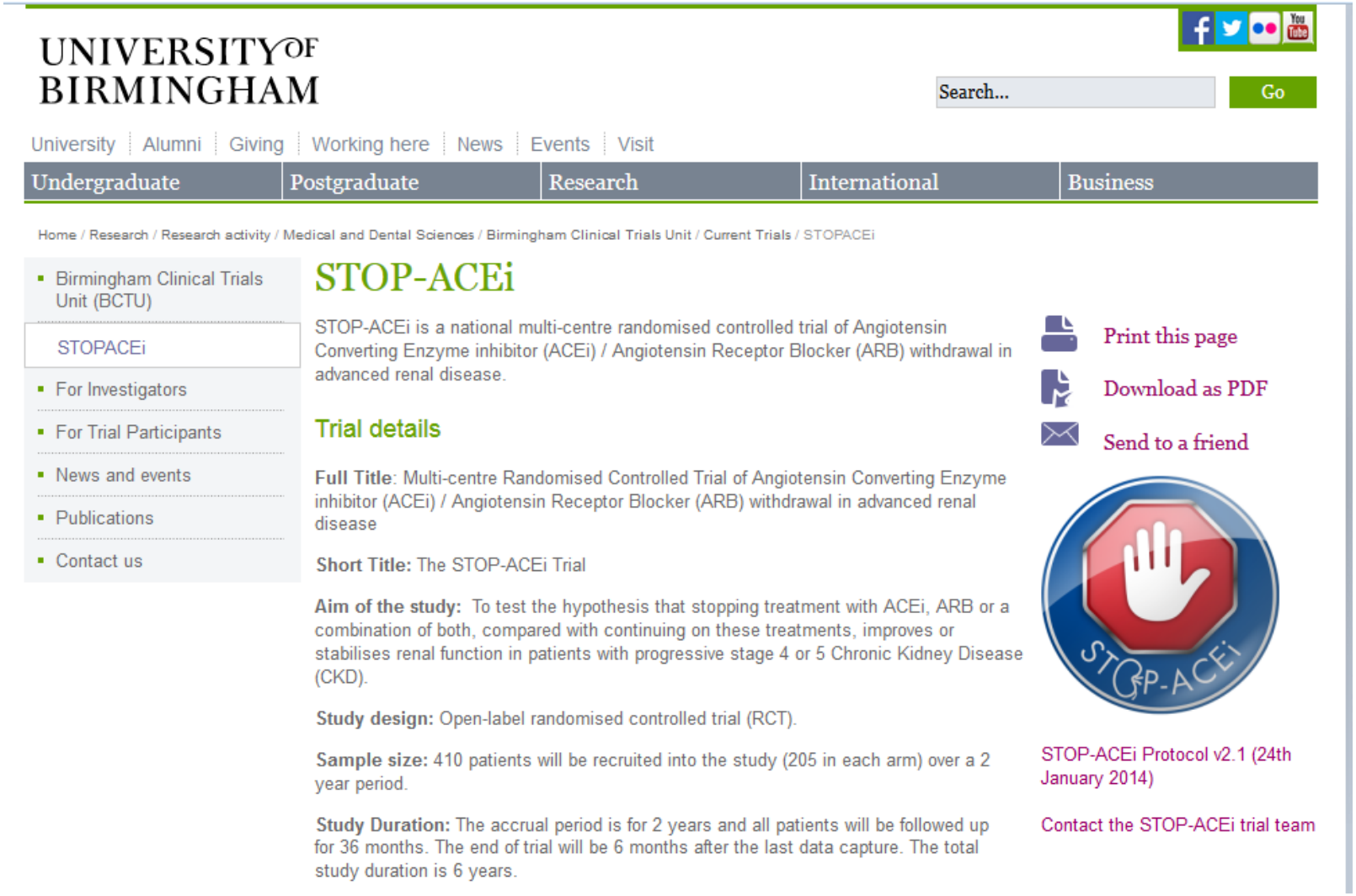


- Please keep originals of CRFs at site.
- Please contact BCTU if you have queries

Pharmacy considerations

- Choice of drugs used is at clinician's discretion
  - ACEi/ARB
  - Other antihypertensives
- Standard Pharmacy stocks used
- No need for additional pharmacy management
  - Accountability logs ✗
  - Study-specific prescription ✗
  - Normal checks and clinical governance ✓

STOP-ACEi website



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STOP-ACEi

STOP-ACEi is a national multi-centre randomised controlled trial of Angiotensin Converting Enzyme inhibitor (ACEi) / Angiotensin Receptor Blocker (ARB) withdrawal in advanced renal disease.

Trial details

Full Title: Multi-centre Randomised Controlled Trial of Angiotensin Converting Enzyme inhibitor (ACEi) / Angiotensin Receptor Blocker (ARB) withdrawal in advanced renal disease

Short Title: The STOP-ACEi Trial

Aim of the study: To test the hypothesis that stopping treatment with ACEi, ARB or a combination of both, compared with continuing on these treatments, improves or stabilises renal function in patients with progressive stage 4 or 5 Chronic Kidney Disease (CKD).

Study design: Open-label randomised controlled trial (RCT).

Sample size: 410 patients will be recruited into the study (205 in each arm) over a 2 year period.

Study Duration: The accrual period is for 2 years and all patients will be followed up for 36 months. The end of trial will be 6 months after the last data capture. The total study duration is 6 years.

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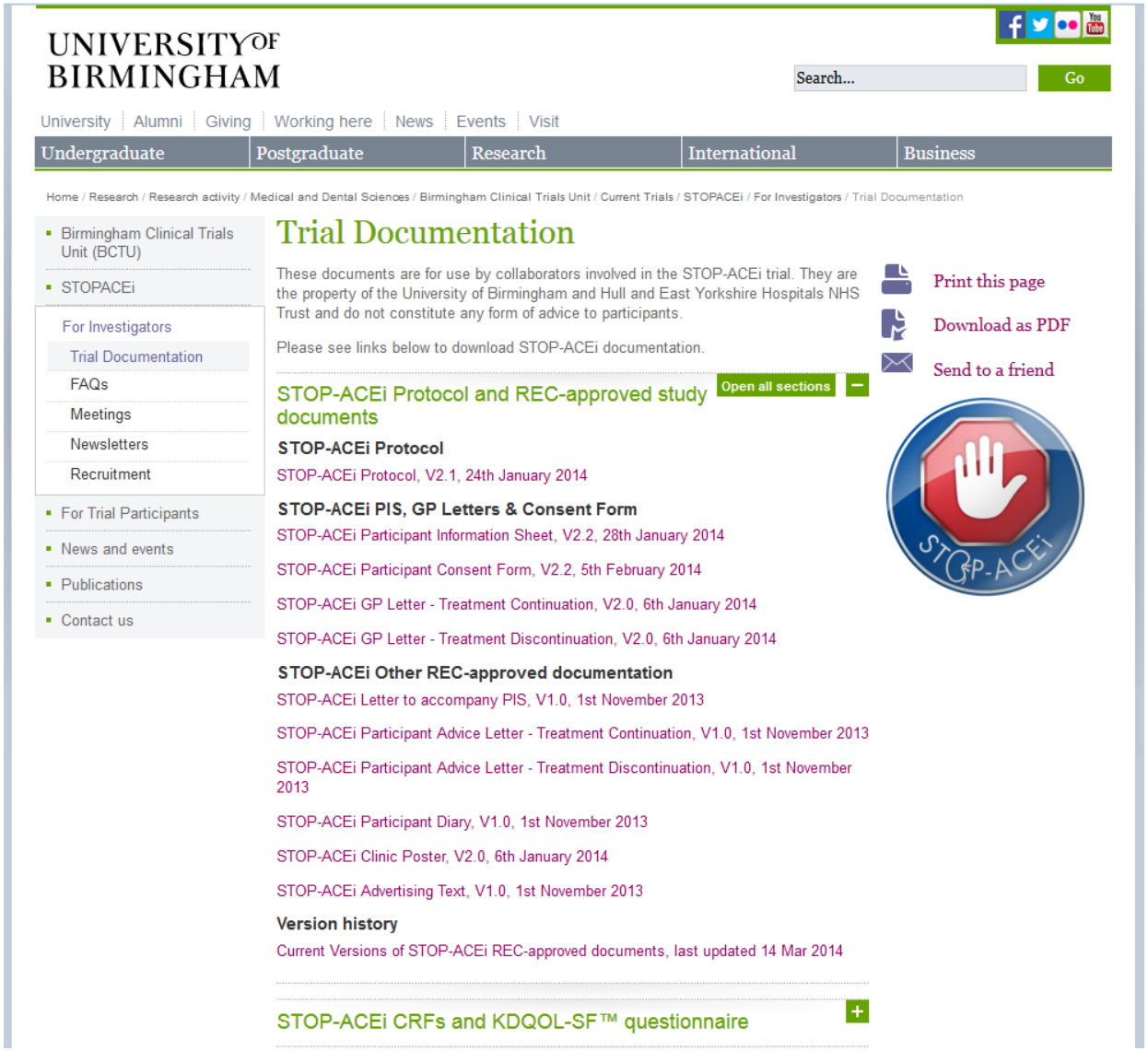
STOP-ACEi Protocol v2.1 (24th January 2014)

Contact the STOP-ACEi trial team

STOP-ACEi website



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Trial Documentation

These documents are for use by collaborators involved in the STOP-ACEi trial. They are the property of the University of Birmingham and Hull and East Yorkshire Hospitals NHS Trust and do not constitute any form of advice to participants.

Please see links below to download STOP-ACEi documentation.

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STOP-ACEi Protocol and REC-approved study documents

Open all sections

STOP-ACEi Protocol

STOP-ACEi Protocol, V2.1, 24th January 2014

STOP-ACEi PIS, GP Letters & Consent Form

STOP-ACEi Participant Information Sheet, V2.2, 28th January 2014

STOP-ACEi Participant Consent Form, V2.2, 5th February 2014

STOP-ACEi GP Letter - Treatment Continuation, V2.0, 6th January 2014

STOP-ACEi GP Letter - Treatment Discontinuation, V2.0, 6th January 2014

STOP-ACEi Other REC-approved documentation

STOP-ACEi Letter to accompany PIS, V1.0, 1st November 2013

STOP-ACEi Participant Advice Letter - Treatment Continuation, V1.0, 1st November 2013

STOP-ACEi Participant Advice Letter - Treatment Discontinuation, V1.0, 1st November 2013

STOP-ACEi Participant Diary, V1.0, 1st November 2013

STOP-ACEi Clinic Poster, V2.0, 6th January 2014

STOP-ACEi Advertising Text, V1.0, 1st November 2013

Version history

Current Versions of STOP-ACEi REC-approved documents, last updated 14 Mar 2014

STOP-ACEi CRFs and KDQOL-SF™ questionnaire

Contact details

Trial website:	www.birmingham.ac.uk/STOPACEi
Online Randomisation and data entry system:	www.trials.bham.ac.uk/STOPACEi
E-mail:	STOPACEi@bham.ac.uk
Telephone:	0121 415 9132
Fax:	0121 415 9135
Post:	Birmingham Clinical Trials Unit, Robert Aitken Institute University of Birmingham Edgbaston Birmingham B15 2TT
STOP-ACEi staff:	Marie Valente, Trial Coordinator Liz Brettell, Renal Trials Manager

Before you leave

- Thank you for coming
- Slides will be made available online
- Certificates
- CPD credits
- Feedback forms
- TMG meeting – Bourneville room