STOP-ACEi Newsletter

Issue 4	Dec 2014

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

Short Title: STOP-ACEi

Welcome to the fourth issue of the STOP-ACEi Newsletter!

Good progress is being made with site set-up. Ten centres are now open to patient recruitment and many more are well on their way.

Trial Design:	**Trial Aim:**
An investigator-led, multi-centre, open-label, randomised controlled clinical trial.	To test the hypothesis that stopping ACEi/ARB treatment, compared with continuing on these treatments, improves or stabilises renal function in patients with progressive stage 4 or 5 chronic kidney disease (CKD).

Population: 410 patients with stage 4 or 5 CKD that have progressive deterioration in renal function (fall in eGFR of >2 mL/min per year over last 24 months) and are currently receiving ACEi/ARB therapy.

New STOP-ACEi recruiting centres

Welcome to all the centres that have recently opened to recruitment. A special mention goes to the teams at **University Hospitals Birmingham**, **Queen Alexandra Hospital Portsmouth**, **Royal Sussex County Hospital** and **Royal Shrewsbury Hospital** for recruiting their first patients. Thank you for your hard work!

Hull and East Yorkshire Hospitals NHS Trust

MRC Medical Research Council

NHS National Institute for Health Research

UNIVERSITY OF BIRMINGHAM

BIRMINGHAM CLINICAL TRIALS UNIT

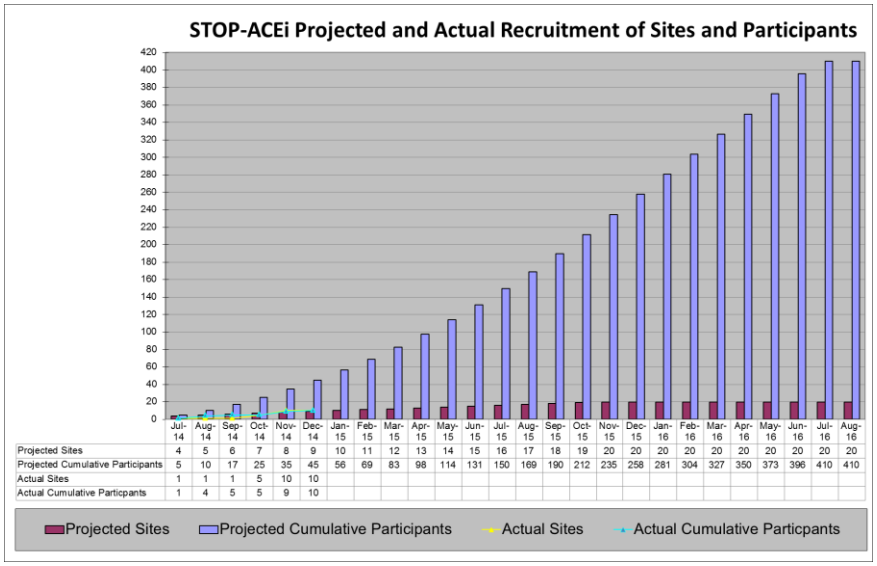
Message from the Chief Investigator

We now have 10 centres open to patient recruitment for STOP-ACEi and more are working hard with trial set-up. Many thanks to all the centres involved for their continued commitment to this important study. We've been struck by the level of enthusiasm for the trial and it's clear that you think the research question is relevant and important so thank you all for your support.

Patient recruitment is underway, but is behind target. It's important we get off to a good start and I hope patient recruitment will pick up as new centres come on board especially with a quick burst pre-Christmas. I am confident with your enthusiasm we will succeed and reach our target early.

Best wishes,
Prof Sunil Bhandari

Recruitment update



	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15	May-15	Jun-15	Jul-15	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Jan-16	Feb-16	Mar-16	Apr-16	May-16	Jun-16	Jul-16	Aug-16
Projected Sites	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	20	20	20	20	20	20	20	20	20
Projected Cumulative Participants	5	10	17	25	35	45	56	69	83	98	114	131	150	169	190	212	235	258	281	304	327	350	373	396	410	410
Actual Sites	1	1	1	5	10	10																				
Actual Cumulative Particpants	1	4	5	5	9	10																				

STOP-ACEi will recruit 410 patients over its 2 year recruitment period. There will be approximately 20 recruitment centres across the UK.

We are behind with recruitment at the moment, but good progress is being made and we hope to make up some lost ground as new centres come on board.

Thank you for your continued efforts with set-up and patient identification.

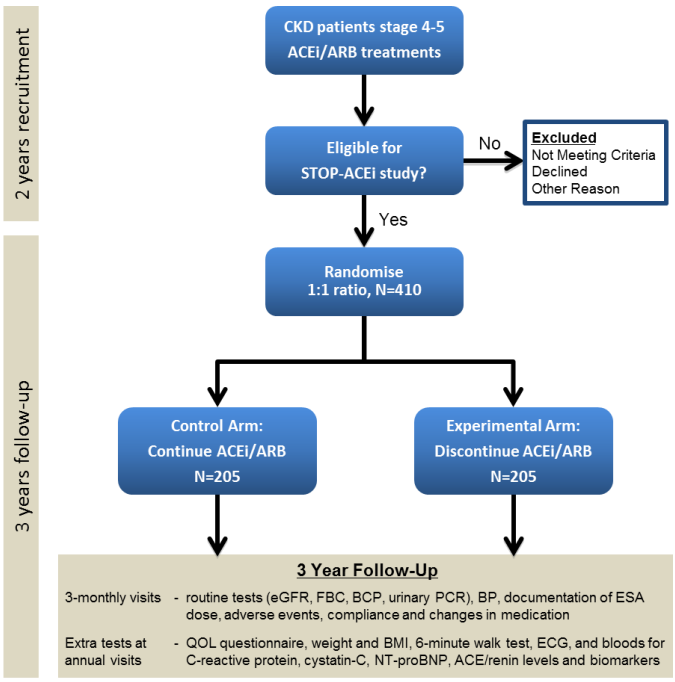
Should ACEi/ARB in patients with cardiovascular comorbidities be discontinued?

It is unknown if these drugs are of benefit in patients with advanced CKD. There are currently no RCTs in this group of patients to demonstrate benefit or harm. One could argue for both sides and more importantly this question has been carefully considered by our independent DMEC committee who will monitor the study closely for adverse cardiac events in both arms of the study and advise if any safety signal appears.

Please update your patient screening and approach logs

With patient recruitment slipping behind target, we're going to be monitoring screening more closely to help identify any avoidable recruitment barriers. If you aren't already doing so, please start updating the Participant Screening Log each time you screen patients (e.g. from a clinic list or patient database) and update the Participant Approach Log each time you send or give a PIS to a patient. We will be requesting a copy of these logs each month starting in the New Year. You can find a copy of these logs in section 3 of your site file.

Study schema



Main Inclusion Criteria

- 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 24 months, a tool to calculate this will be provided);
- 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 ≤160/90 mmHg;
- 3 months of specialist renal follow-up at the time of entry into the trial;
- Written, signed informed consent to the trial.

Please see the study protocol for details.

Setting up STOP-ACEi at your hospital

If you are interested in taking part in the STOP-ACEi trial, the following documents are required for set-up:

- **Practical Arrangements Form**: This form contains some basic feasibility questions. If you would like BCTU to complete the SSI form on your behalf, please fully complete the form. If you will be completing your own SSI form, you need only complete page 3 of the Practical Arrangements Form.
- **Localised study documents**: Please send a copy of the letterhead you want to be put at the head of study documents (e.g. the PIS and consent form) to BCTU and we will adapt these for you.
- **CVs, GCP certificates and honorary staff**: We need CVs (signed and dated within the last 12 months) and up-to-date GCP certificates for all staff that will be working on STOP-ACEi at your site (i.e. all staff named on the delegation log or SSI form). For any staff that do not have a substantive contract of employment with the hospital (e.g. honorary staff), we will also need a Letter of Access or a copy of the honorary contract.
- **SSI form**: This can be completed by yourselves or by BCTU. Please let me know if I can help with completion of the SSI form. Please send a PDF copy of the SSI form to BCTU when it has been fully signed/authorised.
- **Contract**: All sites need a fully signed contract in place before they can open to recruitment for STOP-ACEi. BCTU will provide a template contract which needs to be populated with site-specific information.
- **NHS permission**: Please let us know if we can do anything to help with obtaining local NHS approval. Please send a copy of your R&D approval letter to BCTU when you have it.

Please contact Marie Valente, STOP-ACEi Trial Coordinator at BCTU, if you need any of the above forms or documents, or if you have any questions about trial set-up. We will do everything we can to help.

Online Randomisation System is now LIVE!

Testing has now been completed and the STOP-ACEi randomisation system is now live. To randomise patients into the trial, simply follow the on-screen instructions. You will need all the information in the Randomisation Notepad (CRF01) to enrol a patient into STOP-ACEi.

Some forms are not yet available on the online system, but we hope to release these soon.

Please contact the STOP-ACEi trial office for help and log-in details.

Access the STOP-ACEi online system at: www.trials.bham.ac.uk/stopacei

Your questions answered

Q. Patients with immune-mediated renal disease that requires disease-specific treatment are excluded from STOP-ACEi. Does this include patients on chronic steroids for vasculitis?

A. If patients are deemed by the clinician as stable with inactive renal specific disease then these patients maybe entered.

Q. My patient is unable to do the 6 minute walk test. Can they still participate in the trial?

A. Yes, if a participant is unable to complete the 6MWT, they are still able to continue their participation in the STOP-ACEi trial. A reasonable effort should be made to perform the test for all participants. However, if the responsible clinician feels the test is inappropriate or unsafe for any particular participants, the decision to perform the test is at their discretion.

Q. How long does the STOP-ACEi baseline visit take?

A. This will depend a bit on the patient and local set-up, but will take approximately 3-4 hours: Explanation of study procedure, consent, randomisation – 1 hour; Height, BP, weight – 15 mins; Bloods, KDQOL-SF™, ECG – 1 hour; 6 min walk test – 30 mins; Data entry, central bloods, update casenotes, GP letter etc. – 1 hour. The follow-up assessments should be much shorter.

STOP-ACEi study details:

Sponsor: Hull and East Yorkshire NHS Foundation Trust. Ref: R1578

Funding: The NIHR/MRC Efficacy and Mechanism Evaluation (EME) Programme. Ref: 11/30/07

EudraCT no: 2013-003798-82
ISRCTN no: ISRCTN62869767
REC ref no: 13/YH/0394
IRAS/CSP ref no: 138827

Portfolio adoption: As an NIHR funded study, STOP-ACEi has been adopted onto the NIHR CRN Portfolio.

UK CRN ref no: 15908

The STOP-ACEi study team are always here to help

For further information about the STOP-ACEi trial, please contact us:

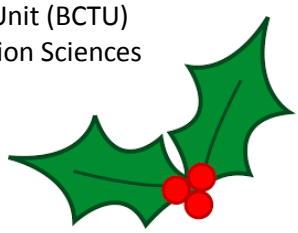
STOP-ACEi Chief Investigator:
Prof Sunil Bhandari, Hull and East Yorkshire Hospitals NHS Trust, sunil.bhandari@hey.nhs.uk

STOP-ACEi Trials Coordinator:
Marie Valente, STOP-ACEi Trial Office, Birmingham Clinical Trials Unit, m.valente@bham.ac.uk

STOP-ACEi Trials Office:
Website: www.birmingham.ac.uk/stopacei
E-mail: STOPACEi@trials.bham.ac.uk
Telephone: (0121) 415 9133
Fax: (0121) 415 9135

Randomisation:
Website: www.trials.bham.ac.uk/stopacei
(online randomisation now open)
Telephone: 0800 953 0274
(Available 9am-5pm, Monday – Friday)

Postal address:
STOP-ACEi Trial Office
Birmingham Clinical Trials Unit (BCTU)
School of Health & Population Sciences
Public Health Building
University of Birmingham
Edgbaston
Birmingham
B15 2TT



BCTU Christmas Closure

Birmingham Clinical Trials Unit, including the telephone randomisation service will be closed from:

16:00, Tuesday 23rd December 2014 until
09:00, Monday 5th January 2015

The online randomisation and data entry service will still be available over the Christmas period.