Progress Review

Launch Meeting

3rd April 2014, Lucas House, Birmingham

BIRMINGHAM CLINICAL TRIALS UNIT

UNIVERSITY OF BIRMINGHAM

Hull and East Yorkshire Hospitals NHS Trust

NHS

Who's involved?

- Grant
  - NIHR/MRC Efficacy and Mechanism Evaluation (EME) Programme
  - Approved 2nd May 2013, Started 1st Feb 2014
  - Ref: 11/30/07

MRC Medical Research Council

NHS National Institute for Health Research

- Sponsorship
  - Hull and East Yorkshire Hospitals NHS Trust

Hull and East Yorkshire Hospitals NHS Trust

NHS

- Coordinating Centre
  - Birmingham Clinical Trials Unit

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BIRMINGHAM CLINICAL TRIALS UNIT BCTU

Approvals

- MHRA
  - Approved 12th December 2013
  - Category A trial
- Ethics
  - Yorkshire and The Humber REC, Leeds East.
  - Protocol version 2.1
  - Approved 29th Jan 2014
- Portfolio adoption
  - Confirmed (pending NHS permissions) 13th Feb 2014
  - Renal speciality group of the CCRN
  - Lead CLRN: The North East Yorkshire and Northern Lincolnshire CLRN

Registries and important numbers

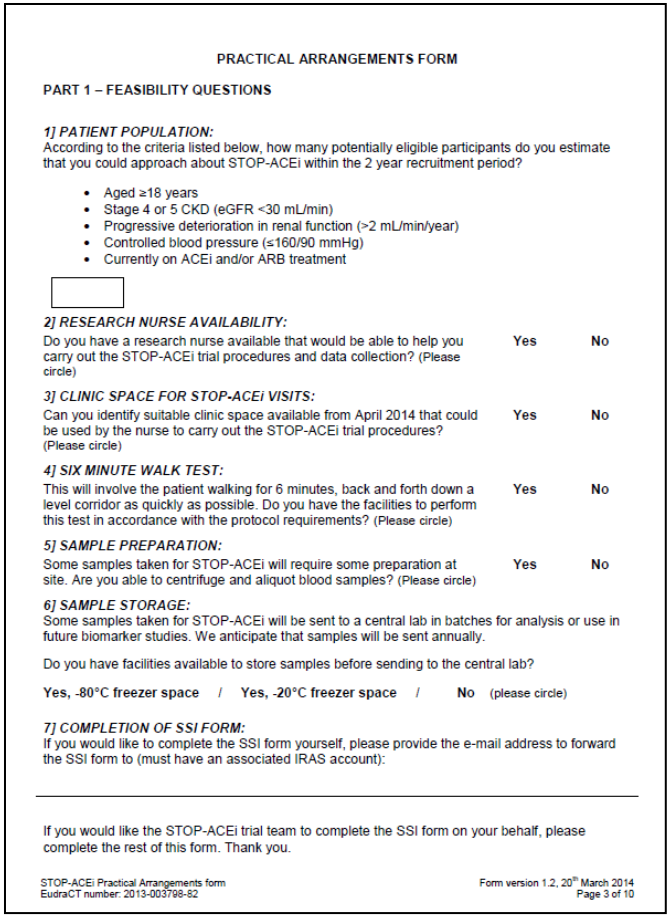
Sponsor reference:	R1578
Funder reference:	11/30/07
REC reference:	13/YH/0394
MHRA CTA reference:	21411/0242/001-0001
ISRCTN:	ISRCTN62869767
EudraCT reference:	2013-003798-82
IRAS project ID:	138827
UK CRN ID number:	15908

Sites

- 23 secondary care sites included in the initial REC application
- 4 main sites
- Set up in progress at several hospitals
- Open to new sites

Site set-up – SSI forms

- Must be listed on the REC form
- Complete Practical Arrangements form
- An SSI form must be completed on IRAS
  - Completed by site – give address on PA form
  - Completed by BCTU – complete all of PA form
- Return PA form to BCTU along with
  - GCP certificates
  - CVs, recently signed and dated
  - Letter head
  - Honorary contracts/Letters of access (if applicable)



PRACTICAL ARRANGEMENTS FORM

PART 1 – FEASIBILITY QUESTIONS

1] PATIENT POPULATION:
According to the criteria listed below, how many potentially eligible participants do you estimate that you could approach about STOP-ACEi within the 2 year recruitment period?

- Aged ≥18 years
- Stage 4 or 5 CKD (eGFR <30 mL/min)
- Progressive deterioration in renal function (>2 mL/min/year)
- Controlled blood pressure (≤160/90 mmHg)
- Currently on ACEi and/or ARB treatment

2] RESEARCH NURSE AVAILABILITY:
Do you have a research nurse available that would be able to help you carry out the STOP-ACEi trial procedures and data collection? (Please circle) **Yes** **No**

3] CLINIC SPACE FOR STOP-ACEi VISITS:
Can you identify suitable clinic space available from April 2014 that could be used by the nurse to carry out the STOP-ACEi trial procedures? (Please circle) **Yes** **No**

4] SIX MINUTE WALK TEST:
This will involve the patient walking for 6 minutes, back and forth down a level corridor as quickly as possible. Do you have the facilities to perform this test in accordance with the protocol requirements? (Please circle) **Yes** **No**

5] SAMPLE PREPARATION:
Some samples taken for STOP-ACEi will require some preparation at site. Are you able to centrifuge and aliquot blood samples? (Please circle) **Yes** **No**

6] SAMPLE STORAGE:
Some samples taken for STOP-ACEi will be sent to a central lab in batches for analysis or use in future biomarker studies. We anticipate that samples will be sent annually.

Do you have facilities available to store samples before sending to the central lab?

Yes, -80°C freezer space / **Yes, -20°C freezer space** / **No** (please circle)

7] COMPLETION OF SSI FORM:
If you would like to complete the SSI form yourself, please provide the e-mail address to forward the SSI form to (must have an associated IRAS account):

If you would like the STOP-ACEi trial team to complete the SSI form on your behalf, please complete the rest of this form. Thank you.

STOP-ACEi Practical Arrangements form
EudraCT number: 2013-003798-82

Form version 1.2, 20th March 2014
Page 3 of 10

Site set-up – Contracts

- All sites need a Clinical Trial Site Agreement (CTSA) in place before the can start any trial activities
- Between Sponsor and the site
- BCTU will coordinate
- Contract is based on the CTSA template
- Includes PI agreement
- Signed by:
  - PI
  - local R&D
  - sponsor R&D

Site set-up – Delegation log

- PI is responsible for the conduct of the study at site
- But, trial duties can be delegated to appropriately trained and capable staff
- The PI is responsible for ensuring that staff are adequately trained and capable of doing their delegated tasks
- This must be documented in the delegation log for ALL staff that do any trial-related activities.

STOP-ACEi Delegation of Duties and Signature Log

Principal Investigator: As PI for STOP-ACEi, signature below confirms that all the delegated duties relating to this project have been listed, that the delegate understands and accepts the responsibilities of their duties and is appropriately trained to carry them out.

Delegate: Signature below indicates that the delegate accepts the responsibilities and believes that the delegated tasks are fully within their capabilities.

Name of delegate please print	**Trial Role** PI, clinician, data manager, research nurse etc.	**Delegated Duties**	**Status**	**Training method**	**Start date** dd/mmm/yyyy	**End date** dd/mmm/yyyy	**Delegate Signature**	**Date of signature** dd/mmm/yyyy	**PI Signature**	**Date of signature** dd/mmm/yyyy
		Please use codes from legend on page 2								
	Principal Investigator									

Site set-up – Training requirement

Minimum training required:

- GCP training
- Study-specific training
  - Protocol review
  - Review of study guidelines – see Section 9 of your ISF
    - Minimum Casenote Documentation Requirements
    - Randomisation and Data Entry
    - Preparation of Trial Samples
    - 6-minute walk test

The study-specific training will be satisfied by:

- Attending the Site Initiation Visit/Teleconference;
- OR Attending a STOP-ACEi Investigator Meeting;
- OR PI-directed training at site;
- OR Self-directed training by reading the study Protocol and applicable guidelines.

Site set-up – Investigator Site Files

- BCTU will provide
- Contains all essential documents
- Useful guidelines and information

- The PI is responsible for maintenance
- BCTU will send updates when needed

Site set-up – Investigator Site Files

Investigator Site File Index

Full 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

Short Title: STOP-ACEi

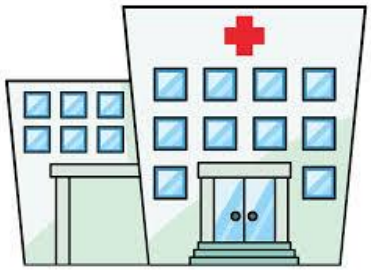
EudraCT No: 2013-003798-82

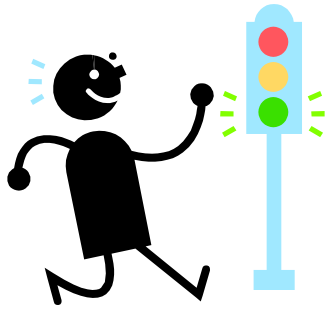
Section	Title	Sub Sections / Comments
1	Study Documentation	(1.1) Important Numbers and Dates (1.2) Current Versions List (1.3) Current Protocol (1.4) Participant Information Sheet (1.5) Informed Consent Form (1.6) GP Letter – Treatment Continuation (1.7) GP Letter – Treatment Discontinuation (1.8) Letter to Accompany PIS (1.9) Clinic Poster (1.10) Advertising Text (1.11) Participant Advice Letter – Treatment Continuation (1.12) Participant Advice Letter – Treatment Discontinuation (1.13) Participant Diary (1.14) Superseded versions of the Protocol (1.15) Superseded versions of the REC-approved Study Documents
2	Sponsorship	(2.1) Sponsorship agreement (2.2) Sponsorship letters
3	Regulatory Approval	(3.1) Original REC application (3.2) Original REC approval letter (3.3) REC amendments approval letters (3.4) Original MHRA Application (3.5) Original MHRA Approval Letter (3.6) MHRA amendment approval letters (3.7) Signed Site Specific Information Form (3.8) Trust site specific R&D approval
4	Subject Documentation and CRFs	(4.1) Subject Screening Log (4.2) Subject Identification Log (4.3) Completed, signed Consent Forms for all Participants (originals) (4.4) Blank Case Report Forms (4.4.1) CRF01: Randomisation Notepad (4.4.2) CRF02: Baseline visit (4.4.3) CRF03: Telephone follow-up (4.4.4) CRF04: 3-Monthly Visit (4.4.5) CRF05: Additional Clinical Visits (4.4.6) CRF10: SAE form
		(4.5) Blank KDQOL-SF™ questionnaire (4.6) Completed Case Report Forms, questionnaires and participant diaries for all Participants (4.7) Superseded Case Report Forms and questionnaires
5	Site Personnel	(5.1) Site Delegation Log - for all research personnel delegated responsibilities by the site PI (original) (5.2) Signed and Dated Current CVs for all Site Personnel (5.3) GCP Certificates for all Site Personnel (5.4) Honorary Contracts / Letters of Access (if applicable) (5.5) Completed Practical Arrangements Form (5.6) Blank Change of Staff Form (5.7) Completed Change of Staff Forms
6	Finance, contracts and Indemnity	(6.1) NIHR/MRC EME Programme Funding Confirmation Letter (6.2) Signed Clinical Trial Site Agreement (Including PI agreement)
7	Serious Adverse Events	(7.1) Blank SAE forms – see ISF section 4.4.6 (7.2) Completed SAE forms (originals) (7.3) SAE definition of expected – see current Protocol section 10 (7.4) SAE Reporting Procedures – see current Protocol Section 10 (7.5) Notification by Sponsor to Regulatory Authorities of SUSARs
8	IMP	(8.1) Electronic Medicines Compendium (eMC) Website Details (8.2) Summary of Product Characteristics examples – Candesartan (ARB), Lisinopril (ACEi) (8.3) Summary of Product Characteristics – Amendments to example SmPCs
9	Study Guides	(9.1) Online Randomisation and Data Entry Guide (9.2) Trial Samples Guide (9.3) Minimum Casenote Documentation Requirements
10	Monitoring	(10.1) Site Initiation Report (10.2) Monitoring/audit reports
11	Reports	(11.1) Final report (11.2) Publication list (11.3) Poster (for clinical staff only, not for advertising to patients)
12	Correspondence	(12.1) Newsletters (12.2) All other correspondence – file in chronological order with the most recent at the front.

Site set-up – Site Initiation Visit

- By teleconference
- Arranged when we have:
  - R&D approval letter
  - Signed CTSA
  - ISF sent received
  - Site staff details
- Afterwards:
  - SIV Report
  - Resolve issues
  - Sponsor green light

Site set-up – Sponsor ‘green light’





Hull and East Yorkshire Hospitals NHS Trust

Site

Prepare SSI or PAF
R&D approval letter
Signed contract
CVs
GCP certificates
Honorary contracts
Letterhead or localised docs
Sign delegation log

BCTU

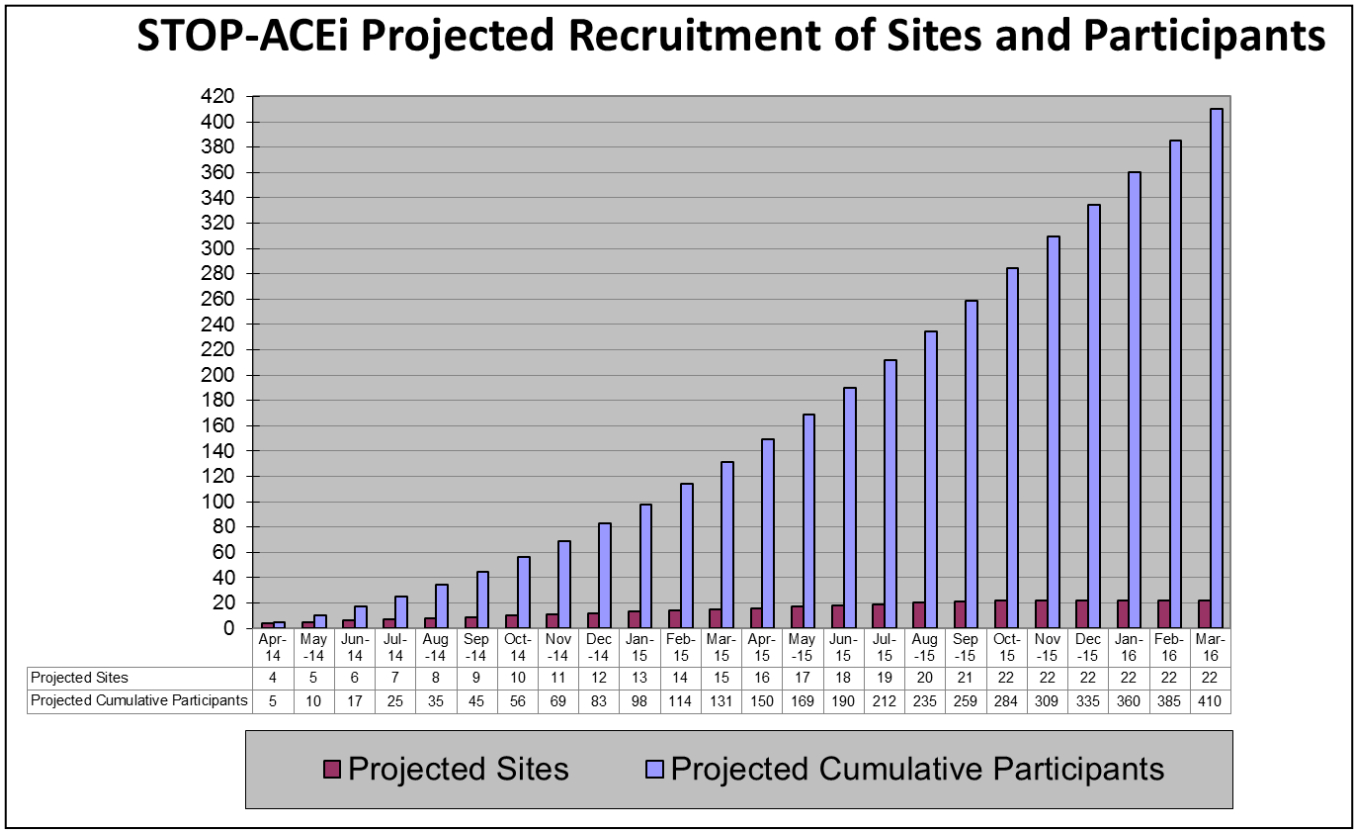
Send ISF
Conduct SIV
Prepare SIV report
Resolve any issues
Apply for green light

Sponsor

RG Checks
Give green light

Recruitment

- Participants: 410 patients
- Centres: 23 included on REC application
- Recruitment duration: 2 years
- Follow-up duration: 3 years



	Apr-14	May-14	Jun-14	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
Projected Sites	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	22	22	22	22	22
Projected Cumulative Participants	5	10	17	25	35	45	56	69	83	98	114	131	150	169	190	212	235	259	284	309	335	360	385	410

Assumes 22 sites recruited at 1 per month and all sites recruiting 1.15 participants per month

Contact details

Trial website:	www.birmingham.ac.uk/STOPACEi
Online Randomisation and data entry system:	www.trials.bham.ac.uk/STOPACEi
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STOP-ACEi staff:	Marie Valente, Trial Coordinator Liz Brettell, Renal Trials Manager