From: "Rebecca Green" <Rebecca.Green@controlled-trials.com>
Subject: **ISRCTN85562386 assigned to your trial (ref: CCT-NAPN-18945)**
Date: 23 September 2009 15:09:57 BST
To: "Sandeep Ankolekar" <Sandeep.Ankolekar@nottingham.ac.uk>, <Philip.Bath@nottingham.ac.uk>
Cc: <wim.clarke@nottingham.ac.uk>

ISRCTN85562386 - Prevention Of Decline in Cognition After Stroke Trial

Dear All,

Our Accounts Department have confirmed your payment. I am therefore pleased to inform you that the following ISRCTN has been assigned to your trial:

ISRCTN85562386 - http://www.controlled-trials.com/ISRCTN85562386

When quoting the ISRCTN, please make sure that no space is inserted between the ISRCTN and the actual number. Please refer to the link below for further guidance notes about how to use the ISRCTN.

http://www.controlled-trials.com/isrctn/sample_documentation.asp

I would also like to remind you that CCT's sister company, BioMed Central (http://www.biomedcentral.com), publishes a wide range of Open Access biomedical journals, in particular the journal Trials, dedicated to publishing protocols, results and other issues relevant to clinical trials. If you would like to publish your trial protocol and/or results papers in Open Access, please visit Trials for more information http://www.trialsjournal.com.

If you have any further questions about the use of the ISRCTN, please do not hesitate to contact me.

Best wishes,
Rebecca

Rebecca Green
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Rebecca.Green@controlled-trials.com
http://www.controlled-trials.com

From: Rebecca Green
Sent: 05 August 2009 12:57
To: 'Sandeep Ankolekar'
Cc: 'wim.clarke@nottingham.ac.uk'
Subject: RE: Confirmation of ISRCTN application (ref: CCT-NAPN-18945)

Dear Sandeep,

Thank you for your email.

Your trial information has been updated, and you will be able to see these changes once your ISRCTN has been assigned and your trial is live on the ISRCTN register. If you would like to make any changes to your trial information once your ISRCTN has been assigned, please do let me know and I will be happy to discuss and implement these changes for you.

Our Accounts Department will send the invoice by email within the next week. If you have not received your invoice within two weeks, please contact me to ensure that this can be resent.

You will be able to pay by credit card, cheque or bank transfer (please note that we do not accept Western Union money transfers). In order to help us track the payment and avoid any delays, could you please ensure that either a copy of the invoice or the invoice number in full is provided?

If payment is by credit card, simply fill in your card details on the invoice and either mail it back to BioMed Central - Springer-Verlag, Post Box 120 141, 14302 Berlin, Germany or email it back to creditcard@springer.com. Credit card payments take up to three working days to process.

If paying by cheque, please make payable to BioMed Central Ltd and mail to our Lockbox address: BioMed Central Ltd., PostBox 20 01 55, 60605 Frankfurt, Germany.

If paying by bank transfer, please use the details provided on your invoice. Bank transfer payments take up to seven working days after the transfer date to be confirmed by our Accounts Department.
Please remember to quote your invoice number as your reference when paying by bank transfer to ensure no delay to your assignation.
Best wishes,
Rebecca

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Rebecca.Green@controlled-trials.com
http://www.controlled-trials.com

From: Sandeep Ankolekar [mailto:Sandeep.Ankolekar@nottingham.ac.uk]
Sent: 05 August 2009 11:50
To: Rebecca Green
Subject: Re: Confirmation of ISRCTN application (ref: CCT-NAPN-18945)

Dear Rebecca,

Thank you for considering the application for ISRCTN registration.

Please note the responses for the queries below. Also I will be most grateful if you could do some minor corrections on the application.

They are :

1. Scientific title:
Could it be slightly altered as follows: Prevention Of Decline in Cognition After Stroke Trial (PODCAST): A factorial randomised controlled trial of intensive versus guideline (moderate) lowering of blood pressure and lipids. (I have deleted lowering at the end of the sentence)

2. Study Hypothesis:
Participants with ischaemic strokes will be randomised to both the blood pressure and lipid lowering arms (in the initial draft I have written it as arm)

Please note the responses for the queries below

1. Could you please confirm the setting (hospital, GP clinic, other) of your trial?

A: Patients will be recruited from hospital based services. Follow up and management will be done by the GP and hospital services and the GP.

2. For your countries of recruitment, I have updated this to read: *'United Kingdom'*, as this is all we require in this section. If your trial becomes international in time, you can update this section as and when each new country is approved and starts recruiting. Could you please confirm that you are happy with this?

A: YES

3. Could you please confirm that your participants are of either sex?

A: YES. They are of either sex

4. As you have stated that you do not have a patient information sheet in web format, then would you be happy with the following standard text to be entered into the Patient information material field to reflect the fact that the Patient Information Sheet (PIS) can be provided by the contact: *'Not available in web format, please use the contact details below to request a patient information sheet*'

A:YES

5. For your interventions section, please provide me with the total duration of treatment and the total duration of follow-up for all arms of your trial.

A: The total duration of the trial is 8 years and follow up for participants will range from 1-8 years depending on the time of enrolment. The trial intervention will be for the same duration.

6. For your primary and secondary outcomes, please provide me with the timepoints at which each of these outcomes will be measured.

A: Primary Outcome : Baseline, 6, 18,30,42,54,66,78,90,96 months
Secondary outcomes:

1. Dementia: **6, 18,30,42,54,66,78,90,96 months**
2. Cognition : All tests at **6, 18,30,42,54,66,78,90,96 months, except tMMSE and TICS-M done at 0,12,24,36,48,70,84 months over the telephone.**

a. Global – MMSE, tMMSE,[28] TICS [29]
b. Association – trail making A/B [30, 31]
c. STROOP test
d. Cognitive decline with/without recurrent stroke
e. Ordinal cognition (MMSE>28/23-28/10-22/<10/dementia/dead)
f. Informant (IQCODE)

3. Quality of life – EuroQoL, informant (DEMQoL) : **Baseline, 6, 18,30,42,54,66,78,90,96 months**
4. Depression (Zung): **Baseline, 6, 18,30,42,54,66,78,90,96 months**
5. Dependency (modified Rankin Scale, mRS): **Baseline, 6, 18,30,42,54,66,78,90,96 months**
6. Disability (Barthel Index, BI) : **Baseline, 6, 18,30,42,54,66,78,90,96 months**
7. Stroke recurrence: **Baseleine and every six months till the end of the trial**
8. Myocardial infarction: **every six months till the end of the trial**
9. Composite vascular events (non-fatal stroke, non-fatal MI, fatal vascular): **Baseline and every six months till the end of the trial**
10. Stroke: fatal/severe non-fatal/mild/TIA/none: **Baseline and every six months till the end of the trial**
11. Myocardial infarction: fatal/non-fatal/angina/none[40] **Baseline and every six months till the end of the trial**
12. Vascular: fatal/non-fatal/none [40] **Baseline and every six months till the end of the trial**
13. New diabetes **Baseline, 6, 18,30,42,54,66,78,90,96 months**
14. New atrial fibrillation **Baseline, 6, 18,30,42,54,66,78,90,96 months**
15. Residence (home, institution), care package, informal family support **Baseline, 6, 18,30,42,54,66,78,90,96 months**
16. Blood pressure (systolic BP, diastolic BP, pulse pressure, rate-pressure product) **Baseline, 6, 18,30,42,54,66,78,90,96 months**
17. Lipids (TC, TG, HDL, calculated LDL) **Baseline, 6, 18,30,42,54,66,78,90,96 months**
18. Neuroimaging (in a subset of participants): **Baseline and at 3 years**

7. We would usually expect the sponsor to be the organisation taking primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting, rather than an individual. In light of this, would *'The University of Nottingham (UK)'* be suitable to name as the sponsor for this trial?

A: YES. University of Nottingham is the Sponsor, but for the UK only.

As you may be aware, there is a cost of £156 per trial. If you could please confirm the name, postal and email address of the person the invoice should be sent to, as well as the VAT (tax) number to quote (*this should be easily gained by contacting your finance department - please note that we are not a VAT-exempt service under medical research*), I shall make sure that our Accounts Department sends this invoice as soon as possible. You will be able to pay by credit card, cheque or bank transfer.

A: Mr Wim Clark
Division of Stroke Medicine
The University of Nottingham
Clinical Sciences Building
Nottingham City Hospital Campus
Nottingham NG5 1PB

E mail: wim.clarke@nottingham.ac.uk

VAT NO: GB 690 3912 25

Thank you very much.

Regards

Sandeep

From: ISRCTN ADMIN [mailto:isrctn@controlled-trials.com]
Sent: 03 August 2009 18:08
To: sandeep.ankolekar@nottingham.ac.uk
Subject: Confirmation of ISRCTN application (ref: CCT-NAPN-18945)

Your trial details have been successfully submitted and your application ref is CCT-NAPN-18945. Please note, however, that **this is not your ISRCTN.**

An ISRCTN will be assigned to your trial once

- it has been checked by the Current Controlled Trials editorial team
- it has been accepted as eligible for registration
- payment has been received.

Payment of the administrative charge is required before an ISRCTN will be assigned. You will be contacted shortly by the Current Controlled Trials staff regarding payment. If you notice any errors in your submission, or if you want to make further changes, please contact the editorial office <mailto:isrctn@controlled-trials.com?subject=ISRCTN APPLICATION CCT-NAPN-18945> .

Click here to return to the Current Controlled Trials homepage <http://www.controlled-trials.com> .

Name: Dr Sandeep Ankolekar
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United Kingdom
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Email: sandeep.ankolekar@nottingham.ac.uk
Where did you hear about the ISRCTN scheme?: University of Nottingham

ClinicalTrials.gov identifier:
Protocol / serial number: version 1.0
Public title: Prevention Of Decline in Cognition After Stroke Trial.
Scientific title: Prevention Of Decline in Cognition After Stroke Trial (PODCAST) : A factorial randomised controlled trial of intensive versus guideline lowering of blood pressure and lipid lowering
Acronym: PODCAST
Study hypothesis: To study if intensive blood pressure and/or lipid lowering post stroke, is better than moderate blood pressure and/or lipid lowering, to prevent cognitive decline after stroke. Participants with ischaemic stroke will be randomised to both the blood pressure and lipid lowering arm; participants with haemorrhagic stroke will be randomised only to the blood pressure lowering arm.
Ethics approval: Applied for Ethics Approval on 24 July 2009 to Nottingham Research Ethics Committee 1
Study design: PODCAST is a multi-centre, prospective, randomised, open-label, blinded end-point, controlled, partial-factorial, phase IV trial.
Countries of recruitment: The trial will have a start-up phase and a main phase. The start-up phase (first 3 years) will assess feasibility, and recruit patients from the UK . The main phase will run for a further 5 years and recruit patients internationally.
Participants - inclusion criteria: 1. Age >70 years and telephone-MMSE >16; or age >60 years and telephone-MMSE 17-19
2. Functionally independent (mRS 0-2)
3. Ischaemic stroke (any cortical OCSP/TOAST type) or primary intracerebral haemorrhage (cortical or basal ganglia)
4. 3-7 months post-event (to allow cognitive, neurological, BP and lipid stabilisation, but avoid attrition)
5. Systolic BP 125-170 mm Hg
6. Total cholesterol 3-8 mmol/l
7. Presence of a reporter: partner, sibling, child, friend (for IQCODE/DEMQoL)

8. Capacity and willingness to give consent
Participants - exclusion criteria: 1. Participants not meeting inclusion criteria
2. Subarachnoid haemorrhage
3. Secondary intracranial haemorrhage (trauma, AVM, cavernoma)
4. Posterior circulation ischaemic stroke
5. Posterior circulation haemorrhage
6. No CT/MRI during index stroke
7. Inability to give consent or do study measures, e.g. severe dysphasia, weakness of dominant arm
8. Severe hypertension (systolic BP>170 mmHg)
9. Definite need for 'intensive' BP control;
10. Severe hypercholesterolemia (TC>8 mmol/l)
11. Definite need for 'high intensity' statin or ezetimibe
12. Definite need for a cholinesterase inhibitor
13. Familial stroke associated with dementia, e.g. CADASIL
14. Chronic renal failure: GFR<50
15. Liver disease, ALT>60
16. Ongoing participation in trials involving drug and/or devices, or within the last 3 months.
Patient information material: Please contact the trial office for further information
Anticipated start date: 01/01/2010
Anticipated end date: 01/01/2018
Target number of participants: 3400 participants (600 in the start-up phase and 2800 in the main phase)
Disease/condition/study domain: Cognitive impairment after Stroke
Interventions: The trial will assess whether intensive blood pressure lowering (systolic blood pressure <125 mm Hg) and lipid lowering (LDL-cholesterol <2.0 mmol/L) is better than moderate blood pressure lowering (systolic blood pressure < 140 mm Hg) and cholesterol lowering (LDL-cholesterol < 3.0 mmol/L).

The study will test management strategies and not individual drugs. Algorithms taking account of 'National Institute of Clinical Excellence, UK Guidelines', relating to stroke, hypertension , lipids and Type 2 Diabetes will aid investigators in treatment decision-making using standard antihypertensive and lipid lowering drugs so that participants are treated as randomised.
Primary outcome measure(s): Comparison of cognition (Addenbrooke's Cognitive Examination extended to include death) between 'intensive' and 'moderate'
BP/lipid lowering groups
Secondary outcome measure(s): For each of BP-lowering and lipid-lowering arms, comparison between 'intensive' and 'moderate' groups:

1. Dementia
a. Using AD - NINCDS/ADRDA and VaD - NINDS-AIREN
b. With/without recurrent stroke
2. Cognition
a. Global – MMSE, tMMSE, TICS
b. Association – trail making A/B
c. STROOP test
d. Cognitive decline with/without recurrent stroke
e. Ordinal cognition (MMSE>28/23-28/10-22/<10/dementia/dead)
f. Informant (IQCODE)
3. Quality of life – EuroQoL, informant (DEMQoL)
4. Depression (Zung)
5. Dependency (modified Rankin Scale, mRS)
6. Disability (Barthel Index, BI)
7. Stroke recurrence
8. Myocardial infarction
9. Composite vascular events (non-fatal stroke, non-fatal MI, fatal vascular)
10. Stroke: fatal/severe non-fatal/mild/TIA/none
11. Myocardial infarction: fatal/non-fatal/angina/none
12. Vascular: fatal/non-fatal/none
13. New diabetes
14. New atrial fibrillation
15. Residence (home, institution), care package, informal family support
16. Blood pressure (systolic BP, diastolic BP, pulse pressure, rate-pressure product)
17. Lipids (TC, TG, HDL, calculated LDL)
18. Neuroimaging (in a subset of participants)
Trial website: http://www.podcast-trial.org
Publications:
Sources of funding: 50:50 Co-funded
The Stroke Association UK : Grant No. TSA2008/09
The Alzheimer's Society UK: Grant No. TSA 2008/09

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