Statins to Ameliorate early onset Pre-eclampsia

Submission date	Recruitment status No longer recruiting
Registration date 08/05/2009	Overall study status Completed
Last Edited 20/05/2019	Condition category Pregnancy and Childbirth

[X] Prospectively registered

- [] Protocol
- [] Statistical analysis plan
- [X] Results
- [] Individual participant data

Plain English summary of protocol

Background and study aims

Pre-eclampsia is a serious condition of pregnancy, where the mother develops high blood pressure and high levels of protein in the urine (proteinuria). There are no effective drug treatments for pregnant women to reverse pre-eclampsia. Drugs can be given to help reduce blood pressure and prevent seizures. Doctors monitor the mothers blood pressure, blood tests and the babys wellbeing and then recommend birth of the baby if the mother or her babys health is threatened. However, if pre-eclampsia develops between 24-32 weeks and the baby is born prematurely, he or she will almost always need special care on a neonatal unit. Recent scientific research has identified that changes in some specific blood chemicals (biomarkers) can lead to pre-eclampsia. Initial studies on samples of placenta and blood vessels, as well as animal experiments, suggest that statins can reduce the level of these blood chemicals, and perhaps reduce or eliminate the effects and risks of pre-eclampsia. This study is the first step in determining if these same beneficial effects are seen in pregnant women.

Who can participate?

Pregnant women with severe pre-eclampsia.

What does the study involve?

Participants do not have to do anything extra if they take part in the study. The pre-eclampsia is managed carefully in the usual way by the same doctors who would normally look after the pregnancy. The only difference is the taking of an extra capsule each day until delivery, either pravastatin or an identical looking placebo (sugar) capsule. This is in addition to any other drugs that the doctors think is appropriate for the pre-eclampsia. Neither the woman nor her doctor can choose which treatment is given. The decision is made randomly by computer at the trial office. This is essential so that a fair comparison can be made between the two treatment groups. Clinical information about the mother and her baby's health is collected from their medical notes every day, including blood pressure, protein in the urine and side effects. Routine monitoring also involves taking regular blood and urine samples, which are also used to measure specific blood chemicals (biomarkers) thought to be important in pre-eclampsia. Permission is also sought to take a sample of blood from the umbilical cord and samples of the placenta following delivery. This is only done if the umbilical cord blood or placenta would otherwise be discarded. The blood samples are used to measure the level of treatment drug. The placenta samples are used to measure specific blood chemicals thought to be important in pre-eclampsia and also to measure the level of treatment drug that passes into the baby's bloodstream. Once

the participant has left hospital, she is asked to come back once or twice, until her baby is 6 weeks old, for check-ups, with further blood samples from the mother.

What are the possible benefits and risks of participating?

All drugs have side-effects, but we do not anticipate any side effects of the study drugs in the relatively short time that they are taken. Statins are taken by millions of non-pregnant people worldwide and side effects are rare. Participants are encouraged to tell their doctor if they feel ill in any way at all, so that the doctor can check to see whether the pre-eclampsia is worsening or if it is a side effect of the drug. Participants may not gain any individual benefit, as only half of the women taking part will receive pravastatin whilst the other half will receive a dummy (placebo) drug. It is hoped that pravastatin will help improve the symptoms and problems associated with pre-eclampsia, so some participants may feel better and their baby may not need to be born early. However, it is not known in advance whether this is the case - that is the reason for doing this study. The main benefit from this study will be that the information gained will help improve the treatment of women with pre-eclampsia in the future.

Where is the study run from? Birmingham Clinical Trials Unit, University of Birmingham (UK)

When is the study starting and how long is it expected to run for? June 2011 to July 2014

Who is funding the study? Medical Research Council (UK)

Who is the main contact? Prof. Asif Ahmed asif.ahmed@aston.ac.uk

Study website

http://www.birmingham.ac.uk/stamp

Contact information

Type(s) Scientific

Contact name Prof Asif Ahmed

Contact details

Aston University Life & Health Sciences Aston Triangle Birmingham United Kingdom B4 7ET

asif.ahmed@aston.ac.uk

Additional identifiers

EudraCT/CTIS number 2009-012968-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers MRC ref: G0701824, MRCIES10215; Sponsor ref: UCLH08/0350

Study information

Scientific Title

A proof of principle, double-blind, randomised placebo-controlled, multicentre trial of pravastatin to ameliorate early onset pre-eclampsia

Acronym

StAmP

Study objectives

The aim of the trial is to establish whether a significant reduction of angiogenic markers by statins will alleviate the severity of early-onset pre-eclampsia (PE) in women. To test this hypothesis, we will ask the following questions:

 Do statins, compared to placebo, inhibit anti-angiogenic factors in women with early-onset PE?
If this principle is established, how best can a substantive trial/health technology assessment be undertaken to develop guidance for routine use of statins in PE?
Are there any adverse effects to the mother or the baby?

Protocol can be found at: http://www.birmingham.ac.uk/Documents/college-mds/trials/bctu/stamp/Stamp-protocol-version-7-0-22-11-2013.pdf

Ethics approval required Old ethics approval format

Ethics approval(s) Wales Research Ethics Committee, 03/09/2010, ref: 10/MRE09/10

Study design Double-blind randomised placebo-controlled trial

Primary study design Interventional

Secondary study design Randomised controlled trial

Study setting(s) Hospital

Study type(s)

Treatment

Participant information sheet

Patient information can be found at: http://www.birmingham.ac.uk/Documents/college-mds /trials/bctu/stamp/Stamp-PIS-version-6-0-22-11-13.pdf

Health condition(s) or problem(s) studied

Pre-eclampsia

Interventions

On 27/09/2010 the drug of treatment was changed to pravastatin; this was previously simvastatin.

Oral pravastatin, 40 mg, or placebo, once daily until delivery of the baby.

Intervention Type

Drug

Phase

Phase IV

Drug/device/biological/vaccine name(s)

Simvastatin

Primary outcome measure

Effect of statins on soluble fms-like tyrosine kinase 1 (sFlt-1) at 48 hours post-randomisation

Secondary outcome measures

Maternal:

- 1. Blood pressure and proteinuria at delivery
- 2. Use of anti-hypertensives during pregnancy and until 1 month post delivery
- 3. Severe morbidity (Haemolysis, Elevated Liver enzyme levels and a Low Platelet count [HELLP], cerebrovascular accident [CVA]). Duration of follow-up: until 1 month post-delivery.
- 4. Days in high dependency unit
- 5. Total hospital stay
- 6. Mortality (up to 42 days post delivery)
- 7. Drug adverse effects during pregnancy

Neonatal outcomes:

- 1. Apgar at 5 min
- 2. Birth weight
- 3. Complications of prematurity (retinopathy, necrotizing enterocolitis [NEC], intraventricular haemorrhage [IVH])
- 4. Days in special care dependency unit
- 5. Mortality up to 28 days old
- 6. Drug adverse effects apparent at delivery
- 7. Congenital anomalies

Overall study start date

01/06/2011

Completion date 31/07/2014

Eligibility

Key inclusion criteria

Current inclusion criteria as of 27/09/2010:

To be eligible for the StAmP Trial, the women must:

- 1. Be between 24+0 weeks' and 31+6 weeks' gestation
- 2. Have a singleton pregnancy

3. Have a diagnosis of early onset pre-eclampsia

4. Be considered capable of safely continuing the pregnancy for 48 hours or more, as determined by the attending clinician

5. Obstetrician and neonatologist believe the fetus is likely to be viable

6. No major anomalies evident on the 20-week anomaly scan. Any anomaly should be assessed by the Principal Investigator and discussed with the Chief Clinical Investigator, following classification of the anomaly according to the ICD-10 codes. All major anomalies will be excluded, but minor anomalies, subject to agreement between the PI and CI will be included

7. Be capable of understanding the information provided, with use of an interpreter if required

8. Give written informed consent

Previous inclusion criteria:

To be eligible for the StAmP Trial, the women must:

- 1. Be at least 24 weeks and less than 33 weeks' gestation (no age limits on participant)
- 2. Have a diagnosis of pre-eclampsia
- 3. Have a normal cardiotocograph
- 4. Be considered capable of safely continuing the pregnancy for 12 hours or more
- 5. Be capable of understanding the information provided, with use of interpreter if required

6. Give written informed consent

Participant type(s)

Patient

Age group

Adult

Sex Fema

Female

Target number of participants 64

Total final enrolment 62

Key exclusion criteria

Current exclusion criteria as of 27/09/2010: Any women, who at the point of randomisation, exhibit any of the following are not eligible for the trial:

1. Eclampsia

2. Current use of statins

3. Contraindications to statin use (other than pregnancy) including:

3.1. Hypersensitivity to pravastatin or any of its excipients

3.2. Active liver disease or elevation of serum transaminases not thought to be related to preeclampsia

3.3. Pre-pregnant renal insufficiency (creatine clearance less than 30 ml/min)

3.4. Concomitant administration of potent CYP3A4 inhibitors

4. Imminent transfer to a non-trial centre due to unavailability of neonatal cots

5. Participation in any other blinded, placebo-controlled trials of investigational medicinal products in pregnancy

6. Significant uncertainty regarding gestational age. Under 24 weeks' gestation, pregnancies are often not considered viable and therefore women with pre-eclampsia less than 24 weeks gestation will be excluded. Women with pre-eclampsia around 32 weeks' gestation are often delivered when the mother is stable and therefore we will exclude women who develop pre-eclampsia over 32 weeks' gestation. For this reason, if there is any uncertainty about the gestational age, the mother should not be approached for randomisation.

Previous exclusion criteria:

Any women, who at the point of randomisation, exhibits any of the following symptoms or contraindications, are not eligible for the trial:

1. Eclampsia

- 2. Absent or reversed end-diastolic flow
- 3. Pre-pregnant or continuing use of statins
- 4. Contraindications to statin use (other than pregnancy)

Date of first enrolment

01/06/2011

Date of final enrolment

31/07/2014

Locations

Countries of recruitment England

United Kingdom

Study participating centre Aston University Birmingham United Kingdom B4 7ET

Sponsor information

Organisation University College London Hospitals NHS Foundation Trust (UK)

Sponsor details

(Chief Investigator: Dr David Williams) c/o Ms Salwa Beydoun Joint UCLH/UCL Biomedical Research and Development (R&D) Unit (1st Floor, Maple House) Ground Floor, Rosenheim Wing 25 Grafton Way London England United Kingdom WC1E 6DB

a.downey@ucl.ac.uk

Sponsor type Hospital/treatment centre

Website http://www.uclh.nhs.uk

ROR https://ror.org/042fqyp44

Funder(s)

Funder type Research council

Funder Name Medical Research Council (UK) (ref: G0701824, MRCIES10215)

Alternative Name(s) Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type Government organisation

Funding Body Subtype National government

Location United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			20/05/2019	No	No
HRA research summary			28/06/2023	No	No