The StAmP Trial:

A Proof of Principle, double blind, Randomised Placebo-Controlled, Multi Centre Trial of Statins to Ameliorate Early Onset Pre-eclampsia.

ISRCTN: 23410175

EudraCT Number: 2009-012968-13

Sponsor Protocol Number: UCL 08/0350

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1. Staff Responsibilities

All personnel involved in trial specific duties with direct contact with trial participants must sign the site *Trial Signature & Delegation Log*. (Personnel involved in obtaining blood samples as part of routine care do not need to sign the log). A copy of the *Trial Signature & Delegation Log* is provided in section 2 of the Site File. The Site File is kept by the Principal Investigator. This form must also be co-signed by the site's Principal Investigator. Once complete, a copy of the form must be returned to the StAmP Trial office. The original must be retained in section 2 of the Site File. New site personnel accepting responsibilities can then be added to the form if required.

Please ensure that the StAmP Trial office is informed of any changes in the contact details for the responsible staff. Should the responsible staff change, the *Trial Signature & Delegation Log* must be updated as necessary and forwarded to the StAmP Trial office.

2. Sample Collection Schedule

	Baseline (Prior to treatment)	Treatment Period				Delivery	Postnatal Period	
		Day 1	Day 2	Day 3	Twice weekly until delivery	Day of Delivery	Twice weekly until discharge	6-week follow-up
Blood Samples	X	X	X	X	X	X	X	X
mRNA Samples	X			X				
Urine Samples	X			X		X		
Cord Blood Sample						X		
Placenta Sample						X		

2.1 Blood Samples

As a minimum, blood samples need to be collected from the patient at the following time points:

- At baseline (before treatment has started)
- Daily for the first three days of treatment
- Twice a week thereafter until delivery
- At delivery
- Twice a week postnatally until discharge from hospital
- At 6-weeks postnatally.

These samples should be taken at the same time as routine sampling wherever possible, however where this is not possible, additional samples may occasionally need to be taken specifically for the trial.

These samples will be used to determine the level of inflammatory and anti-angiogenic factors including sFlt-1, PlGF, and sENG.

2.2 mRNA Samples

Two samples need to be collected at baseline and on day 3 of treatment only. These are in addition to the blood samples in section 2.1.

These will be used to determine the level of heme oxygenase-1 (HO-1) expression.

2.3 Urine Samples

Three samples need to be collected - at baseline and on day 3 of treatment and at delivery.

These will be used for the analysis of inflammatory and anti-angiogenic factors including s-Flt-1 and PlGF.

2.4 Cord Blood

A cord blood sample needs to be collected on the day of delivery. This should only be collected if the umbilical cord blood would otherwise be discarded.

This sample will used to determine the level of pravastatin crossing the placenta.

2.5 Placenta Sample

A sample of placenta needs to be collected on the day of delivery. This should only be collected if the placenta would otherwise be discarded.

3. Supplies

Each site will be supplied with kits (one kit per recruited patient) containing the following:

- 5ml cryotubes and coloured caps for processed specimens
- PAXgene tubes (x2)
- Sample storage box.
- Pre-printed labels

When you have 3 sample kits remaining, please complete a **Sample Kit Request Form** (Appendix 1) and fax it to the StAmP Trial Office on 0121 415 9136. More kits will be despatched immediately.

The following equipment is required but not provided:

- Venepuncture kit
- Standard citrated vacutainers
- Centrifuge
- Pipettes
- -80 ^{o}C Freezer (or -20 ^{o}C if not available).

4. Quality Assurance of the Samples

Please complete the sample collection information log (Appendix 2) for each sample taken. This information is necessary for us to ensure the integrity and quality of the samples.

The following information is required:

- Patient Trial Number, initials and date of birth. One log sheet can be completed for each patient.
- Date of sample
- Time of sample. **USE 24 HOUR CLOCK** (e.g.14 45)
- Time centrifuged. **USE 24 HOUR CLOCK** (e.g.14 45)
- Time frozen. **USE 24 HOUR CLOCK** (e.g.14 45)
- Name and signature of the person preparing the sample

Use continuation sheet if first sheet is full and ensure to add page number to the footer.

Ensure any completed logs are forwarded to the StAmP Trial Office as per instruction.

5. Sample Preparation

5.1. Blood Samples

- Approximately 5-10ml of blood drawn into standard citrated (light blue top) vacutainers.
- Invert the vacutainer 3-4 times. The filled vacutainer may be stored at room temperature for no longer than 2 hours prior to centrifugation.
- Centrifuge the blood sample at ~1,500g at 4^{o}C for 15 min. Do not exceed 3,000g. This will produce about 2-5 ml of plasma.
- Within 30 minutes of centrifugation, using a pipette transfer the plasma in a 5ml cryotube. Take care not to disturb the cell pellet.
- Label the tube with the correct pre-printed label provided. Please complete the date of birth, patient initials and the date of sample.
- Put the sample into the small sample box provided.
- Place samples into the freezer (in sample box) at -80^{o}C (or -20^{o}C if not available).
- You will be contacted to arrange collection of the samples by a courier. All transport packaging and dry ice will be provided.
- On arrival at the central laboratory, the samples will be stored at -80^{o}C until analysis.

5.2. mRNA Samples

- Approximately 2.5ml of blood drawn into pre-labelled PAXgene vacutainers. The PAXgene vacutainer contains the buffers required for storage and must be kept upright during sampling. The blood sample should be taken via a butterfly/tube and not directly via a needle into the PAXgene vacutainer.
- Label the tube with the correct pre-printed label provided. Please complete the date of birth, patient initials and the date of sample.

- The tubes must be stored upright at room temp for over 2 hours (maximum of 72 hours) then stored in a freezer at -80°C (or -20°C if not available).

5.3. Urine Samples

- Approximately 5ml of urine needs to be collected and put in a 5ml cryotube.
- Label the tube with the correct pre-printed label provided. Please complete the date of birth, patient initials and the date of sample.
- Put the sample into the small sample box provided.
- Place samples into the freezer (in sample box) at -80°C (or -20°C if not available).
- You will be contacted to arrange collection of the samples by a courier. All transport packaging and dry ice will be provided.
- On arrival at the central laboratory, the samples will be stored at -80°C until analysis.

5.4. Cord Blood Sample

- 1-5ml of venous umbilical cord blood drawn into standard citrated (light blue top) vacutainers. This will produce between 0.55-2.75 ml of plasma.
- Centrifuge at ~1,500 g at 4°C for 15 min. Do not exceed 3,000g.
- Within 30 minutes of centrifugation, transfer the plasma to a clean 5 ml cryotube.
- Label the tube with the correct pre-printed label provided. Please complete the date of birth, patient initials and the date of sample.
- Put the sample into the small sample box provided.
- Place samples into the freezer (in sample box) at -80°C (or -20°C if not available).
- You will be contacted to arrange collection of the samples by a courier. All transport packaging and dry ice will be provided.
- On arrival at the central laboratory in Edinburgh, the samples will be stored at -80°C
- The cord blood sample will later be transferred to UCL for analysis.

5.5. Placenta Sample

- A $1cm^2$ full thickness biopsy of placenta is needed.
- Transfer the sample to a 5ml cryotube.
- Label the tube with the correct pre-printed label provided. Please complete the date of birth, patient initials and the date of sample.
- Snap freeze the sample in liquid nitrogen.
- Put the sample into the small sample box provided.
- Place samples into the freezer (in sample box) at -80°C
- You will be contacted to arrange collection of the samples by a courier. All transport packaging and dry ice will be provided.

- On arrival at the central laboratory in Edinburgh, the samples will be stored at -80°C until analysis.

6. Sample Labelling

All trial centres will be provided with sheets of pre-printed labels for the sample tubes.

TNO: 1001, Day 00 barcode:IIIIII
Patient DOB: __/___/____
Patient Initials:_____
Sample Date:__/___/_____

All samples should be labelled with a pre-printed label. **Please ensure you use the correct label with the correct trial number, type of sample and day of sample**.

All should be completed with patient date of birth, patient initials and date of sample.

7. Sample Storage

Samples should be stored in a pre-labelled StAmP sample storage box until the patient has completed her involvement in the trial (after the 6-week post-partum sample collection). The size of the sample box is approximately 133 mm x 133 mm x 95 mm.

7.1. Storage Conditions

All prepared trial samples should be stored in a freezer at a temperature of -80°C (or -20°C if not available).

7.2. Temperature Deviation

Trial samples should be stored at -80°C (or -20°C if not available).

Provision must be in place to store the samples within the permitted temperature range. Temperature must be monitored regularly. Ideally, a continuing electronic monitoring system (24/7) is expected. However it is acceptable to use a well maintained system of max min thermometer recording at least once per working day.

Temperature logs should be maintained at all times. Temperature logs must be available for inspection by the monitoring team, when requested at monitoring visits.

Should there be a deviation in the storage temperature of the trial samples **above -5°C**, the StAmP trials office should be notified immediately of the deviation and site will be instructed accordingly. The deviation must be recorded on the Temperature Deviation Form, copies of which are provided in section 6.

8. Transportation of Samples to Edinburgh

Samples will be collected once the patient has completed her involvement in the trial (i.e. after the 6-week post-partum sample collection). The centre will be contacted to arrange collection of the samples by a courier. All transport packaging and dry ice will be provided.

A designated site contact for the courier will be required for each participating site. Details should be given to the StAmP Trial Office (stamp-trial@contacts.bham.ac.uk).

The centre will be contacted prior to each sample collection to agree a date and time with the courier. The courier will require details about the location of the laboratory storing the samples.

In the morning of the sample collection day, the courier will deliver to the named contact the transport box and sufficient dry ice for the samples.

The named contact will place all of the samples collected in the transport container with the dry ice and seal the container.

The courier will collect the sealed container and deliver it next day to the laboratory in Edinburgh.

9. Monitoring

The StAmP Trial will be monitored by the StAmP Trial Coordinator from the StAmP Trial Office. Monitoring may also be performed by representatives of UCL as the Sponsor or representatives of the regulatory authorities.

The Monitor Visit Report for each monitoring visit will be filed in section 9 of the Site File. The Monitor Visit Report documents activities performed and issues noted by a Monitor during an on-site monitoring visit.

Please file follow up letters from monitoring visits also in section 9 of the Site File.

Thank you for your valued support of the StAmP Trial

10. Contacts

Should you have any queries or require further information, please contact:

Professor Asif Ahmed (Chief Non-Clinical Investigator)
Centre for Cardiovascular Science,
University of Edinburgh Queen's Medical Research Institute
47 Little France Crescent
Edinburgh
EH16 4TJ
☎: **07973 553123**
✉: **a.s.ahmed@ed.ac.uk**

Or Louise McDougall on **Louise.McDougall@ed.ac.uk**

Alternatively, please contact

Laboratory Coordination
Dr Peter Hewett
School of Clinical and Experimental Medicine
University of Birmingham
Birmingham
B15 2TT

☎: **0121 4142659**
✉: **p.hewett@bham.ac.uk**

StAmP Trial Office
Trial Coordinator – Miss Alex Furmston
Birmingham Clinical Trials Unit
Robert Aitken Institute
University of Birmingham
Edgbaston
Birmingham
B15 2TT

☎: **0121 415 9112**
FAX: 0121 415 9136
✉: **stamp-trial@contacts.bham.ac.uk**

When contacting, please include the following information:

- **Your name, email address and telephone number**
- **Your site details (including department and full address**
- **Patient Trial Number – if applicable**

APPENDIX 1 - SAMPLE KIT REQUEST FORM

THE STAMP TRIAL

A Proof of Principle Double-Blind Randomised Placebo-Controlled Multi-Centre Trial of pravaStatin to Ameliorate Early Onset Pre-eclampsia

SAMPLE KIT REQUEST FORM

When you have 3 sample kits remaining, please complete this form and fax it to:

StAmP Trial Office on 0121 415 9136

(PLEASE PRINT DETAILS)

Contact Name:	_____
Email Address: _____	Telephone Number:
Hospital: _____	
Address: _____	
_____	
_____	

Please tick as required

	Yes	No
Complete Kit	☐	☐
Cryotubes	☐	☐
PAXgene	☐	☐
Sample storage boxes	☐	☐
Pre-printed labels	☐	☐

APPENDIX 2 - SAMPLE COLLECTION INFORMATION LOG

THE STAMP TRIAL

A Proof of Principle Double-Blind Randomised Placebo-Controlled Multi-Centre Trial of pravaStatin to Ameliorate Early Onset Pre-eclampsia

SAMPLE COLLECTION INFORMATION LOG

StAmP Trial Number		Mother's Initials	_____	Mother's date of birth	DD/MMM/YYYY

Blood Samples Sample ID	Date of Sample	Time sample taken (24 hours)	Time Centrifuged (24 hours)	Time Frozen (24 hours)	Name of Nurse/Technician (CAPITAL LETTERS)	Signature	Comments
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			

mRNA Samples Sample ID	Date of Sample	Time sample taken (24 hours)	Do NOT centrifuge	Time Frozen (24 hours)	Name of Nurse/Technician (CAPITAL LETTERS)	Signature	Comments
	DD/MMM/YYYY	HH/MM		HH/MM			
	DD/MMM/YYYY	HH/MM		HH/MM			

Urine Samples Sample ID	Date of Sample	Time sample taken (24 hours)	Do NOT centrifuge	Time Frozen (24 hours)	Name of Nurse/Technician (CAPITAL LETTERS)	Signature	Comments
	DD/MMM/YYYY	HH/MM		HH/MM			
	DD/MMM/YYYY	HH/MM		HH/MM			

Cord blood Sample Sample ID	Date of Sample	Time sample taken (24 hours)	Time Centrifuged (24 hours)	Time Frozen (24 hours)	Name of Nurse/Technician (CAPITAL LETTERS)	Signature	Comments
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			

Placenta Sample Sample ID	Date of Sample	Time sample taken (24 hours)	Do NOT centrifuge	Time Frozen (24 hours)	Name of Nurse/Technician (CAPITAL LETTERS)	Signature	Comments
	DD/MMM/YYYY	HH/MM		HH/MM			

Please return this form to: StAmP Trial Office, FREEPOST RRKR-JUZR-HZHG, Birmingham Clinical Trials Unit, School of Cancer Sciences, University of Birmingham, Birmingham, B15 2TT
Tel: 0121 415 9112; Fax: 0121 415 9136; Email: stamp-trial@contacts.bham.ac.uk; Website: www.stamp.bham.ac.uk

Continuation sheet for additional blood samples

StAmP Trial Number		Mother's Initials	_____	Mother's date of birth	DD/MMM/YYYY

Blood Samples Sample ID	Date of Sample	Time sample taken (24 hours)	Time Centrifuged (24 hours)	Time Frozen (24 hours)	Name of Nurse/Technician (CAPITAL LETTERS)	Signature	Comments
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
	DD/MMM/YYYY	HH/MM	HH/MM	HH/MM			
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