The StAmP Trial:
A Proof of Principle, Double-Blind, Randomised
Placebo-Controlled, Multi-centre Trial of
pravaStatin to Ameliorate Early Onset Pre-eclampsia

Patient Information Sheet

QUICK SUMMARY

- You have been diagnosed with pre-eclampsia, which is a potentially serious condition of pregnancy.
- In order to have the best outcome for your pregnancy and to plan the most appropriate time for
  child-birth you will be admitted to hospital and will be under observation until the baby is born. In
  some cases, you may be treated as an outpatient with frequent visits to hospital, rather than being
  admitted to hospital. We will still monitor you closely until your baby is born.
- Currently, there is no effective treatment for pre-eclampsia except birth of the baby. Premature
  child-birth may lead to medical problems for the new born baby.
- You are being invited to take part in a clinical trial of pravastatin, which belongs to a class of
  medicines called ‘statins’, that might improve your condition and delay the need for your baby to be
  born early.
- If you do decide to take part, there will be a 50:50 chance of receiving either pravastatin or a dummy
  capsule (placebo). Neither you nor your doctor will know beforehand which treatment you will
  receive; this will be determined at random, after you have made a decision to join the study.
- Statins are not normally given to pregnant mothers. However, the medicines safety watchdog has
  agreed that pravastatin can be given as part of this study because they agree any potential risk from
  taking this medicine may be outweighed by the benefits of pravastatin to the pregnancy.
- If you want to take part in the trial, treatment is likely to be most effective if started as soon as
  possible, so you will need to make a decision as soon as possible and ideally within 24 hours of
  diagnosis.

We understand this is a difficult time for you to make such an important decision, but if you think you
might be interested in the study, please read the rest of this leaflet. The names of the people who can
answer any further questions are given below.

LOCAL HOSPITAL StAmP TRIAL RESEARCH STAFF CONTACT DETAILS

OBSTETRICIAN:....................................................... TEL: .........................

RESEARCH MIDWIFE:............................................... TEL: ..........................
PART ONE of this leaflet tells you about the purpose of the StAmP trial and what will happen if you take part.

PART TWO gives you more detailed information about the conduct of the study.

PART ONE

Invitation to participate in the StAmP trial

You are invited to take part in a research study to find out whether a class of drugs called statins can help improve the outcome of pregnancies affected by severe pre-eclampsia. This study is called StAmP (pravaStatin to Ameliorate early onset Pre-eclampsia) and compares one type of statin (pravastatin) with a dummy treatment (placebo). The study is entirely voluntary – you do not have to take part, nor do you have to give a reason if you decide not to participate. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it would involve. Please take your time to read this information sheet carefully and talk to others about the study if you wish. If there is anything that is not clear, or if you would like more information, you should ask your obstetrician or the research midwife for further advice.

What is a pre-eclampsia?

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 will monitor your blood pressure, blood tests and the baby’s wellbeing and then recommend birth of your baby if your or your baby’s 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.

What is the purpose of the study?

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. The StAmP study is the first step in determining if these same beneficial effects are seen in pregnant women.

Why have I been asked to take part?

You have been referred by your GP, midwife or an outpatient clinic doctor to a specialist maternity doctor because you have raised blood pressure and protein in your urine, which means you have pre-eclampsia. You will have other blood tests and an ultrasound to review the wellbeing of your baby. This will help assess the severity of the pre-eclampsia and whether your baby needs to be born. You will be admitted to hospital today so that your condition can be continually monitored. In some cases, you may be not be admitted to hospital and will be treated as an outpatient instead but we will still monitor you closely until your baby is born.

We aim to recruit 64 pregnant women with severe pre-eclampsia from hospitals all over the UK to this study.

Do I have to take part?

You do not have to take part. It is up to you to decide. If you do not wish to take part, you do not have to give a reason and your decision will not affect the standard of care you will receive. Similarly, if you do decide to take part, you are entitled to withdraw from the study at any time, without having to give a reason, and this will not affect the standard of your medical care in any way. Whether you take part or not, you are likely to receive drugs to lower your blood pressure and you and your baby will be closely monitored in hospital.
If I take part will I have pravastatin or the placebo treatment?

Neither you nor your doctor can choose which treatment you receive. The decision is made randomly by computer at the StAmP trial office. This is essential so that a fair comparison can be made between the two treatment groups. Dividing people into groups in this way is called a ‘randomised clinical trial’ and it is the standard and most reliable way of comparing different treatments. There is an equal chance of being allocated to the pravastatin group or the dummy drug (placebo) group.

In addition, neither you nor your obstetrician or midwife will know which of the groups you will be in throughout your pregnancy. This is called a ‘double blind randomised controlled trial’.

What will happen to me if I take part?

You will be asked to take one capsule every evening until your baby is born. This is in addition to any other drugs that the doctors looking after you think is appropriate for your pre-eclampsia.

What will I have to do?

You will not have to do anything extra if you take part in the study. Your pre-eclampsia will be managed carefully in the usual way by the same doctors who would normally look after your pregnancy. The only difference will be the taking of an extra capsule each day until delivery, either pravastatin 40mg or an identical looking placebo (sugar) capsule. Clinical information about you and your baby's health will be collected from your medical notes every day, including your blood pressure, protein in your urine and side-effects. Some clinical data collected may also be used in an associated study to look at factors predicting complications and outcomes for pre-eclampsia.

Routine monitoring will also involve taking regular blood and urine samples and we may occasionally need to take an additional sample for the purposes of this study. The blood and urine samples will be used to measure specific blood chemicals (biomarkers) thought to be important in pre-eclampsia.

We may also request your permission to take a sample of blood from the umbilical cord following delivery. This will be used to measure the level of treatment drug. We will only do this if the umbilical cord blood would otherwise be discarded. Therefore, your baby’s health will not be compromised in any way by taking this sample of umbilical cord blood.

We may also request your permission to take up to four samples of placenta following delivery. This will be 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 your baby’s bloodstream. We will only collect this sample if the placenta would otherwise be discarded. Therefore, your or your baby’s health will not be compromised in any way by taking this sample.

Once you have left hospital, we may ask you to come back once or twice, until your baby is 6 weeks old, for check-ups, with further blood samples. We will not take blood from your baby for the study at any time.

All biological samples will be anonymised, analysed and stored at Aston University. Cord blood samples will later be analysed at University College London.

What are the side effects of treatment received when taking part?

All drugs have side-effects, however we do not anticipate any side effects of the study drugs in the relatively short time that you will be taking them. Statins are taken by millions of non-pregnant people worldwide and side effects are rare. If you do feel ill in any way at all, you must tell your doctor, who will check to see whether the pre-eclampsia is worsening or you are having a side effect of the drug.

Are there any benefits for me from taking part in the study?

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. We hope pravastatin will help improve the symptoms and problems associated with pre-eclampsia, so you may feel better and your baby may not need to be born early. However we cannot be sure in advance whether this is the case – that is the reason for doing this.
trial. The main benefit from the StAmP trial will be that information gained from the trial will help improve the treatment of women with pre-eclampsia in the future.

**What are the possible risks and disadvantages of taking part?**

Statins are used to lower cholesterol in people at risk of heart attacks. Statins have never been formally tested in pregnant women and are therefore not normally given during pregnancy. Nevertheless, for several reasons, many pregnant women have taken statins in pregnancy. We have conducted a thorough review of all reported cases where women have continued to take statins whilst pregnant. Overall statins did not cause any more abnormalities to babies compared with babies born to mothers who did not take statins. In particular, no abnormalities were seen with pravastatin. However there were too few reported cases for us to be absolutely sure that there is no risk of harm. To minimise any risk, we will closely monitor you and your baby’s health throughout the trial and will keep you fully informed.

The Medicines and Healthcare Products Regulatory Authority (an agency of the Department of Health which regulates medicines in the UK) have looked at this review and other information from animal experiments and have concluded it is acceptable to use pravastatin in pregnancies affected by severe pre-eclampsia in the context of this study.

There are many different brands of statin. We have chosen to use pravastatin as it is less likely to cross the placenta to the baby than the other types of statin. We will be keen to check whether this is true by taking a blood sample from the baby’s umbilical cord at birth and measuring the level of pravastatin.

**If you are interested in the StAmP Trial, the next section provides more information.**
PART TWO

What if new information becomes available?

To protect patients’ safety, an independent committee of experts will review the results of the StAmP trial on an ongoing basis, as well as information from other relevant trials. This is so that if statins unexpectedly turn out to be worse than the standard, that would be detected as soon as possible and the trial stopped.

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your doctor will tell you about it and discuss with you what to do next. If you decide to withdraw, you and your doctor will decide your future care. If you decide to continue in the study you will be asked to sign an updated consent form.

What will happen if I don’t want to carry on with the study?

If you do decide to take part, you can withdraw from the study at any time and stop taking the study treatment, without having to give a reason, and this will not affect the standard of your medical care in any way. However if you do withdraw, we would still like to follow up your and your baby’s progress. An important aim of the trial is to find out how many women complete their treatment and how women get on if they withdraw from treatment. For this reason, we would like to keep all data and samples collected up to the point of stopping treatment and we would like to continue to collect a few important details such as when your baby is born and the symptoms of pre-eclampsia. In the unlikely event of you losing the ability to give continued consent during the study, we would like to keep data that we have already collected about you for research purposes.

What if there is a problem?

Every care will be taken in the course of this clinical trial. Whether or not you take part in this trial, you would retain the same legal rights as any other patient treated in the National Health Service. However in the unlikely event that you or your baby are injured by taking part, compensation may be available.

If you suspect that the injury is the result of the Sponsor’s (University College London) or the hospital’s negligence then you may be able to claim compensation. After discussing with your trial doctor, please make the claim in writing to Dr David Williams who is the Chief Investigator for the clinical trial and is based at University College London. The Chief Investigator will then pass the claim to the Sponsor’s Insurers, via the Sponsor’s office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

You may also be able to claim compensation for injury to you or your baby caused by participation in this clinical trial without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your trial doctor in the same way as above.

If you are not satisfied with any aspect of the way you have been approached or treated during the course of this study, you should first speak to the researchers (contact details are on the front cover of this information sheet) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, the normal National Health Service complaints mechanisms are available to you: ask to speak to the complaints manager for the Hospital.

Will information about me be kept confidential?

Yes, all information collected in the study will be kept strictly confidential in the same way as your other medical records. If you agree to take part, doctors involved in your medical care will collect medical information about you, your baby and both your condition and send it to the StAmP Trial Office at the University of Birmingham Clinical Trials Unit (BCTU), on paper and electronically, where it will be securely stored under the provisions of the 1998 Data Protection Act and/ or applicable laws and regulations. Information held by the NHS may be used to follow your progress. Your GP, and other doctors involved in your
clinical care, will be kept informed, but otherwise all information about you, your baby and your treatment will be kept confidential.

If you take part in the trial, your relevant medical records may be inspected by authorised individuals from the BCTU and from the sponsor of the trial (University College London). They may also be looked at by regulatory authorities. The purpose of this is to check the trial is being carried out correctly.

In line with Good Clinical Practice Regulations, at the end of the study, the data will need to be securely archived for at least 5 years (but ideally not less than 15 years). Arrangements for confidential destruction will then be made.

**What will happen to the results of the research study?**

When the results of the StAmP study are known they will be published in medical journals and the results circulated to medical staff and participants. No individuals will be identified.

**Involvement of the General Practitioner/Family doctor**

With your consent we will inform your GP of your participation in the StAmP Trial.

**Who has organised, reviewed and funded the research?**

The StAmP Trial is funded by the Medical Research Council. The Clinical Trials Unit at the University of Birmingham will collect and analyse the data and Aston University will store and analyse the blood samples. The trial is sponsored by University College London. The research has been reviewed by all these organisations and a Multicentre Research Ethics Committee. The Medicines and Healthcare Products Regulatory Authority have approved the use of pravastatin in pregnant women in this trial.

The doctors involved are not being paid for recruiting women into the study. Patients are not paid to take part either, but their help in finding out more about how best to treat pre-eclampsia is much appreciated.

**Do you have any further questions?**

Having read this leaflet, it is hoped that you will choose to take part in the StAmP study. Please keep this copy of the StAmP Trial Patient Information Sheet. You will also be given a copy of your signed consent form to keep if you decide to participate in the StAmP trial.

If you have any questions about the study now or later feel free to ask your specialist or the research midwife. You may also find it helpful to contact Action on Pre-eclampsia (Helpline: 0208 427 4217 Mon-Fri 10-3; Address: 2C The Halfcroft, Syston, Leicester, LE7 1LD; Website: www.apec.org.uk). They know about the study and all about pre-eclampsia.

Thank you for taking the time to read this Participant Information Sheet about the StAmP Trial.