Patient Information Leaflet – PIPIN Study

Your questions answered:
This leaflet contains information about the PIPIN study and helps to answer questions which are commonly asked by people who take part in research. Research is conducted in all areas of health to help improve knowledge and understanding and improve the experience of health care for patients.

The research team who spoke to you today are doctors and midwives who work in Pregnancy Research. They are interested in finding treatments that may help reduce preterm birth and they are trying to improve outcomes. Today you are being invited to take part in a research study. Taking part may not benefit you or improve your pregnancy outcomes but it may help women in the future.

Before you decide whether you would like to take part, it is important for you to understand why the research is being done and what this involves. **Please read this leaflet and ask the doctor or midwife questions, if you require more information.**

What is the PIPIN study?
The PIPIN study is investigating whether women who are in preterm labour or at high risk of delivering before 37 weeks gestation would be willing to take a tablet to try and stop the labour and improve baby health. Pravastatin is the tablet we would like to compare with a placebo (dummy tablet). We are trying to find out if taking Pravastatin might help to prevent pre-term delivery and offer some protection for the baby.

Why have I been asked to join?
Your Doctor or Midwife has identified you as being in preterm labour or having a high risk of delivering your baby before 37 weeks.

Do I have to take part?
It is your choice to take part or not you do not have to take part if you do not want. If you do decide to take part you can withdraw at any time from the study without giving any reason. If you do not take part or later withdraw from the study, it will not affect your care or any treatment plans.

What does the study involve?
If you agree to take part, you will be asked to sign a consent form. We will also ask for your consent to access you and your baby's medical notes and to contact you in the future for up to 5 years after the study has ended.

After consent we will do some blood tests, taking around 10ml (or two teaspoons) once, and 4x 5mls (or a teaspoon) over the next days. We may also ask you to have a vaginal ultrasound scan to measure the length of your cervix (the neck of your womb). Depending on the results of these (which we will discuss with you) you will then be randomised (allocated to either Pravastatin or a placebo tablet). Neither you nor your doctor will be told which tablet (pravastatin or placebo) you have been given.

You will then take one tablet each day, for 7 days. During the first 7 days we will take bloods twice on day one; then once each on day two and day seven (four times in total). Where possible, we will take these at the same time as routine blood samples you may require and/or from your IV line (a plastic tube that may be inserted into your arm to take blood and give medications) if you have one. When you deliver your baby, we would also like to take a small sample of blood from the umbilical cord, which is attached to the placenta. We will also ask you record your experience and report how you are each day in a diary.

28 days after the date your baby was due to be delivered (your EDD), we will check your medical records to collect some information about you and your baby's well-being. We will also contact you to ask you a few questions about your experience of being in the study. This can be via email, telephone or via post, whichever is easiest for you.

In total, you could be taking one tablet each day for up to 7 days, during which time we would like you to tell us how you are feeling in your study diary. You will see a member of the research team on day 7, and will also be contacted at, or around your due date to answer a questionnaire about how your experience of the research has been.

If additional funding is available in the future, we may wish to contact you after 2 years and find out about your and your baby's health. We would contact you at the time via your preferred method of contact to ask your permission for this.

** Please note, this medication is NOT suitable for patients with a lactulose intolerance (due to the powder which makes up the drugs), and the capsules contain gelatine of BOVINE **(cow)** origin. **

What are statins, and why are we using them in preterm labour?
Statins have been widely used to lessen the risk of heart disease by reducing cholesterol (fat cells in the blood), but they have also been shown to reduce inflammation. We know that inflammation is a cause of preterm labour, and statins have been shown to reduce inflammation and slow or stop contractions in preterm labour in laboratory experiments.

What are the risks to me?
Statins have never been formally tested in pregnancy, and because of this, are usually contraindicated - meaning that we would not routinely prescribe this treatment. Lots of information has been collected from women who have accidentally taken statins whilst pregnant, and several studies investigating Pravastatin for the prevention of conditions like pre-eclampsia have been performed. There have been no reports of harm to mothers or their babies from taking pravastatin during pregnancy. There are still too few cases for us to absolutely guarantee no risk of harm, but we will monitor you and your baby's health very closely during this study and will keep you fully informed.
The Medicines and Healthcare Regulatory Authority (a government agency that makes sure medicines are used safely in the UK) have looked at this study and others like it, and concluded that it is safe to use pravastatin in this way.

A few patients (around 3 in 1000) taking this medication have reported tummy upset, including diarrhoea, heartburn, dizziness or sleep disturbance. Very rarely (less than 1 in 10,000 patients taking the medications), statins can cause a problem with muscles or reversible problems with the liver. We will monitor your bloods very closely for this and would stop treatment immediately if you show any sign of these rare complications.

Will this affect my baby?
Pravastatin does not cross the placenta and we know from previous studies in pregnancy that it appears to be safe for babies.

What are the benefits to me?
There may not be any benefits to you, but we hope that the results of this study may help pregnant women in the future.
Will this change the treatment I would normally have?
Pravastatin is usually safe to take with treatments that your doctor may need to prescribe. There is a potential for some antibiotics to interact with Pravastatin but we will discuss this with you and your doctor before you start, or if you need to be prescribed antibiotics during the study.

Will I need any extra tests?
If your doctor thinks that you are at risk of preterm labour but has not been able to take a swab called fetal fibronectin, we will perform a vaginal ultrasound to look at the length of your cervix. This takes a few minutes. Whilst you are in hospital with possible preterm labour, you would normally have daily blood tests – we would collect additional blood for the PIPIN study at the same time. We will take these blood tests from your drip where possible.

When you do deliver, we would like to take a small blood sample from the umbilical cord attached to the placenta. This is to look at inflammation in the blood coming from your baby.

When we have tested all of these blood samples, we will store them in the Edinburgh Reproductive Tissue Bio Bank, located in the Queen's Medical Research Institute, in an anonymous fashion. They may be used in the future in ethically approved pregnancy-related research, including testing for DNA, but they will not be able to be traced back to you. Detailed information about the Bio Bank is available in the separate Edinburgh Reproductive Tissue Bio Bank (ERTBB) Patient Information Sheet. Consent for your samples to enter the Bio Bank is taken separately. During the study, only members of the PIPIN research team will have access to your samples. If at any point you wish for your samples to be removed from the PIPIN study and destroyed, this can be arranged through the research team. After PIPIN has ended, if you wish for your samples to be removed from the Bio Bank and destroyed, this can be arranged via the Bio Bank directly. Unless otherwise instructed, other researchers may have access to your samples in an anonymous fashion for future research.

Will this keep me in hospital longer?
Any patient with threatened preterm labour may be kept in hospital for 2 days or longer for monitoring. Your Doctor will explain this to you and will decide when it is suitable for you to go home. When you go home we would ask that you continue to take the medication and that you return to hospital on day 7 to meet with the study team for one further blood test and to check on how you are. This visit will take around 30 minutes, this appointment may also be arranged as a home visit if you prefer.

Will I know if I am taking the drug?
No. This is a double-blinded, randomised controlled study. This means that neither you nor any of your doctors know which tablet you have been given; pravastatin or the placebo.

Will the information about me and my baby be confidential?
Yes, any information that we collect will be kept confidential and no personal information will be used in any publication.
With your permission, we would like to collect some personal details. These will include: your Community Health Index (hospital) number, your address and date of birth. The Community Health Index (CHI) is a population register, which is used in Scotland for health care purposes. The CHI number uniquely identifies a person on the index. This is so we can contact you at the end of the study with information about the results, including your treatment and in the future, if you agree. Your consent form and study number will be stored securely in the Clinical Study Trial office at the Queen's Medical Research Centre, University of Edinburgh.

We must also inform your GP that you are taking part in the study.
Can I take part in other research?
Please let the research team know if you have consented to take part in other research projects. This is important as some projects are not suitable for you do at the same time as PIPIN.

Who is organizing and funding the research?
This study is led by Professor Jane Norman and is funded by Tommy's Charity. Tommy's Charity supports medical research nationwide looking into miscarriage, stillbirth and premature birth and how we can help women and their babies. More information can be found at www.tommys.org.

Who has reviewed this study?
The East of Scotland Research Ethics Service REC 2, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from the University of Edinburgh and NHS Lothian, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

What if there is a problem?
If you have a concern about any aspect of this study, you should speak with the researcher who will do their best to answer your questions. If you remain unhappy and wish to formally complain, you can do this through the NHS complaints procedure. Please contact NHS Lothian:

Patient Experience Team,
NHS Lothian
2nd Floor
Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG
Tel: 0131 536 3370

In the unlikely event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against NHS Lothian but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

What will happen to the results of the study?
At the end of the study, we will be able to inform you of the study results if you wish. The results will be published in medical journals. You will not be identified in any report/publication. All information related to clinical studies in pregnancy is kept in secure storage for at least 25 years.

Thank you for reading this information leaflet and for considering whether to take part in this study.

If you would like further information please contact:

Dr. Eleanor Whitaker (Clinical Research Fellow)
Email: Eleanor.Whitaker@nhs.net
Telephone: 0131 242 6613 (Research Office)

OR
Dr. Sarah Stock (Principal Investigator)
Email: sarah.stock@nhs.net

OR
Sonia Whyte (Trial Manager)
Email: Sonia.whyte1@nhs.net
Telephone: 0131 242 2693

If you would like to take to an independent obstetrician (i.e. one not involved in this trial) to discuss the trial, please contact:

Professor Fiona Denison

Consultant Obstetrician
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