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PARTICIPANT INFORMATION LEAFLET ***FIBRONECTIN TESTING***

Helping you decide whether or not to join our study

1. Study Title

Does progesterone prophylaxis to prevent preterm labour improve outcome? – A randomised double blind placebo controlled trial. "OPPTIMUM".

Short title: Does progesterone to prevent preterm labour improve outcome?

2. Invitation Paragraph

You are being invited to take part in a research study, as you have been identified by your doctor or midwife as someone who may be suitable. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. What is the purpose of the study?

The purpose of the study is to see if progesterone given to women at high risk of preterm delivery is good for mother's and baby's health. However in order

to know if you are suitable to enter the study we need to do a fibronectin test. This information leaflet is to tell you about fibronectin testing.

Fibronectin is a substance made naturally by the body in pregnancy, and binds the fetal membranes (around the amniotic fluid) to the lining of the womb. If it is found in high quantities in your vagina in pregnancy, you are more likely to deliver preterm. The fibronectin test measures the amount of fibronectin in the vagina.

If you are fibronectin positive you will be eligible for the main study to see if giving progesterone to women at high risk of preterm delivery is good for both the mother's and baby's health. Regardless of the fFN result, you will also be eligible if you had a previous spontaneous labour resulting in a preterm birth ≤ 34 weeks gestation or short cervix in index pregnancy, defined as cervical length ≤ 25mm, but we would like to find out whether the fibronectin test is positive, as this will help us determine the group of women that progesterone works best in.

Information on the main study is available in a separate sheet and will be given to you if you are eligible, or would like further information before deciding whether or not to participate in the screening.

4. Why have I been chosen?

You have been chosen because we believe you might be at higher than average risk of preterm delivery. This may be because of what happened in a previous pregnancy, or because you have been found to have a short cervix on ultrasound. We would like now to do a fibronectin test to check whether you really are at high risk of preterm delivery. If the fibronectin test is positive, then we believe your risk of having a preterm delivery is around 4 in 10. We will then ask if you would like to participate in the main study.

If your fibronectin test is negative, this means that you are at lower risk of preterm delivery, and you will not be eligible for participation in the main study unless you have a spontaneous labour resulting in a preterm birth ≤ 34 weeks

gestation in a previous pregnancy or a short cervix in index pregnancy, defined as cervical length ≤ 25mm in this pregnancy.

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5. **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

6. **What will happen to me if I take part?**

If you agree to take part we will take a swab from your vagina. The swab will then be tested for "fibronectin". You will be informed of the results and, if appropriate, you will be invited to participate in the main study looking at a treatment that we hope will reduce the risk of having your baby early. Whatever the result of your fibronectin test, we will follow you up to see how many weeks pregnant you are when you have the baby, how your baby is delivered, and your own and your baby's health details at delivery.

7. **What do I have to do?**

We ask that you agree to a vaginal swab for the fibronectin test to be performed. Once the fibronectin test is completed, you will be informed of the results and, if appropriate, you will be invited to participate in the main study and given further information.

Women who are not randomised to progesterone or placebo will be provided with a (pre paid) postcard to let us know when they have delivered their baby. The local care team will then collect information from your hospital notes about you and your baby's, delivery; such as the date and type of delivery. Information collected will help us to evaluate the outcomes for all women who were considered at risk of preterm delivery and will contribute towards the understanding we have about preterm labour.

8. What is the drug, device or procedure that is being tested?

The drug that is being tested in the main study is called progesterone. There is some evidence to suggest that it might be helpful in preventing preterm delivery but further research is needed to understand its long term effects. This information form is for the fibronectin testing part of the study only.

9. **What are the alternatives for diagnosis or treatment?**

At present, there are no licensed or recommended treatments for the prevention of preterm delivery in women at high risk in the UK.

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

At this stage you will not be given any treatment with medication but information is available in the leaflet about the main study. You can request the leaflet from your doctor or view it on our website, www.opptimum.org.uk

11. What are the other possible disadvantages and risks of taking part?

A vaginal swab can be a little uncomfortable.

12. **What are the possible benefits of taking part?**

We will be able to give you a clearer idea of how likely you are to have a preterm delivery. In the event that you are at high risk of preterm birth, you would be eligible for participation in the main study.

13. **What happens when the research study stops?**

At the end of the study in 2015, the results will be published on the study website and in medical journals.

14. What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Please direct complaints to the local research doctor in the first instance.

15. What will happen if I don't want to carry on with the study?

You can withdraw from treatment at any time. The information collected up

until the point you decide not to continue will be used.

16. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

In the 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 (the local Hospital or the Study Sponsors: University of Edinburgh/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).

17. Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential.

With your consent we will notify your own GP of your participation in the study. We may also ask your GP how you and your baby are getting on in the future. This may happen, approximately every five years from the time that your baby reaches the age of 5 years.

The data will be stored for following NHS guidelines: at least 25 years and possibly longer.

18. What will happen to any samples I give?

The fibronectin test will be done using the vaginal swab. The swab will be destroyed thereafter.

19. Will any genetic tests be done?

No.

20. What will happen to the results of the research study?

The results of the study will be published in a medical journal, and on the study website in due course (www.opptimum.org.uk). You will not be identified in any report/publication.

21. Who is organising and funding the research?

The study is being funded by the UK Medical Research Council: NIHR Efficacy and Mechanism Evaluation (EME). It is organised and sponsored by the University of Edinburgh/NHS Lothian. The sponsors of this study will contribute to the expenses of the hospital for including you in this study.

22. Who has reviewed the study?

This study was given a favourable ethical opinion for conduct in the NHS by the Scotland A Research Ethics Committee.

23. Who should I contact?

If you are interested in participating in Opptimum or would like further information, please contact:

Name of local Doctor _____

Hospital: _____

Address: _____

_____

_____

Telephone: _____

Email: _____

You will be given a copy of this information sheet and a copy of your signed consent form to keep.

Thank you for or taking time to read this sheet and for considering taking part

b)

LOCAL LOGO TO BE INSERTED

Opptimum
Progesterone prophylaxis to prevent pre-term labour

PARTICIPANT INFORMATION LEAFLET (MAIN)

Additional Information to help you decide whether or not to join the treatment part of our study

1. Study Title

Does progesterone prophylaxis to prevent preterm labour improve outcome? – A randomised double blind placebo controlled trial "OPPTIMUM".

Short title: Does progesterone to prevent preterm labour improve outcome?

2. Invitation Paragraph

You are being invited to join the treatment part of the Opptimum study;, before you decide to participate it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask your doctor if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. What is the purpose of the study?

The purpose of the study is to see if giving progesterone to women at high risk of preterm delivery is good for mother's and baby's health. We plan to look at your health during your pregnancy and the baby's health until the baby is two years of age. We will also ask you to complete questionnaires about your experience of using the treatment. These questionnaires will also ask

about you, and your baby's, health following the pregnancy, in order to assess the effects of giving progesterone. It is possible these questionnaires may also indicate if this treatment is costly or money-saving for the NHS.

4. **Why have I been chosen?**

You have been invited because the fetal fibronectin test was positive or because you had a spontaneous preterm labour resulting in a birth ≤ 34 weeks gestation or a short cervix in this pregnancy, (defined as cervical length ≤ 25mm) and we therefore believe that you might be at higher than average risk of preterm delivery. Fibronectin is a substance made naturally by the body in pregnancy. It binds the fetal membranes (around the amniotic fluid) to the lining of the womb. If it is found in high quantities in your vagina in pregnancy, you are more likely to deliver preterm.

We hope that 1250 women in your situation will agree to participate in the study, of whom 625 will be treated with progesterone and 625 will be treated with a placebo (dummy) treatment.

5. **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and will be asked to sign another consent form. You are free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the care you receive.

6. **What will happen to me if I take part?**

Sometimes we don't know which way of treating patients is best. To find out, we need to make comparisons between different treatments. We do this by putting people into groups and give each group a different treatment; the results are then compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly). The results are then compared.

If you agree to take part we will give you a pack of study medication. The

study medication is in the form of a capsule. The capsule will either contain progesterone or a “placebo”. A placebo is a “dummy treatment”, which looks like the genuine medicine but contains no active ingredient. One capsule should be inserted into the vagina every evening before going to bed, using your finger.

The study doctor / midwife will write down the date you should start medication and also when to stop taking the medication; this will be recorded in the patient diary we will ask you to keep. Most women will start taking the treatment between 22 and 24 weeks of pregnancy. All women will be asked to stop taking the treatment when they are 34 weeks pregnant.

You will not know which treatment group you are in. The trial is a double blind trial, and so neither you nor your doctor will know which treatment group you are (although, if your doctor needs to find out he/she can do so).

We hope that you will agree to stay in this study until after you have had your baby. Participation in this study may require around three extra visits to hospital during your pregnancy, each of which will last 30 minutes. During this time you will have a check up and will be asked some questions about your health. We will also ask you to fill in questionnaires to tell us how you are getting on, after you have had your baby. We may also ask you to take part in an interview telling us what you think about your experience of using the treatment. We will collect some information from your medical notes about your health.

We would also like to collect information about the baby’s health. We can (with your permission) get most of this from the baby’s notes. We will ask your permission to do an ultrasound scan of the baby’s head when he / she is born and ask you to fill in further questionnaires when your baby is approximately one year old, to tell us about their health and experience. Additionally, we would like to see your baby again when he / she is two years old to see how he / she is getting on.

Lastly, we would like your permission to contact you in the future to see how your baby gets on as he / she grows up; and to access information in health records about you and your baby. We cannot be certain when this would happen, but it may be approximately every five years from the time that your baby reaches the age of 5 years.

7. **What do I have to do?**

We ask you to take the study medication as directed, and attend the extra clinic visits we invite you to. We also ask that you complete the study related diary and questionnaires.

8. **What is the drug, device or procedure that is being tested?**

The drug that is being tested is called progesterone. There is some evidence to suggest that it might be helpful in preventing preterm delivery but further research is needed to understand its long term effects. The treatment dose being tested is 200mg (one capsule) per day inserted in to the vagina every evening.

9. **What are the alternatives for diagnosis or treatment?**

At present, there are no licensed or recommended treatments for the prevention of preterm delivery in women at high risk.

10. **What are the side effects of any treatment received when taking part?**

These are unlikely but possible side effects of this treatment are: acne, flushing, rashes, fluid retention, weight changes, tummy upset, changes in libido, breast discomfort, migraine, tiredness and premenstrual symptoms. If you agree to participate in the main study and have side effects that concern you, please contact the local study team.

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

The other disadvantage is the inconvenience for you in making extra hospital visits during your pregnancy, completing questionnaires and bringing your child in for follow up studies in the future.

12. **What are the possible benefits of taking part?**

We cannot promise the study will help you but the information we obtain might help improve the treatment of women with a high risk of preterm delivery in the future.

13. What happens when the research study stops?

At the end of the study in 2015, we will be able to inform you of the study results if you wish. If you wish us to do so, please inform your study doctor. The results will also be published on the study website and in medical journals. We will keep the information about you for as long as possible: at least 25 years.

14. What will happen if I don't want to carry on with the study?

You can withdraw from treatment but you may wish to keep in contact with us to let us know your progress. If you do withdraw from treatment, the information already collected about you will still be used. We are required to follow up each case, to collect information about your pregnancy up until the time your baby is born. We will collect this information from your notes, unless you tell us otherwise.

15. **What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak with the local researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

In the 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 (your local hospital or the Study Sponsors: University of Edinburgh/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).

16. **Will my taking part in this study be kept confidential?**

Yes, all information that is collected about you during the course of the research will be kept strictly confidential. The Medical Research Council: NIHR Efficacy and Mechanism Evaluation (EME) who fund this study may ask us to share the information with other approved researchers; however, your identity (eg name, date of birth) will not be passed on.

We plan to send the details of you and your baby to the National Health Service Care Register (NHSCR) so that we can be informed of any major illnesses that you or your baby have in future. In order to be able to contact you about your own and your baby's health in future, your name and contact details, those of a relative or friend, and your GP details will be requested. These contacts will be kept securely, with access restricted on a secure database managed by the University of Glasgow. This information will be used only to contact you about the study by the study doctor or researchers running this trial. You will not be named or otherwise identified in any study publication.

In addition, with your consent we will notify your own GP of your participation in the study. We may also ask your GP how you and your baby are getting on in the future.

17. **Will any genetic tests be done?**

Yes. Once you have had the baby we would like your permission to store a sample of the placenta (afterbirth) and placental DNA. We may keep some of these samples in a tissue bank for future research. Ethical permission will be sought for any future research projects. Although the placenta may need to be examined as part of your care, it is optional whether you agree to the use of the surplus tissue and DNA for future research.

18. What will happen to the results of the research study?

The results of the study will be published in a medical journal, and on the

study website in due course (www.opptimum.org.uk). You will not be identified in any report/publication.

19. Who is organising and funding the research?

The study is being funded by the NIHR Efficacy and Mechanism Evaluation (EME). It is organised and sponsored by the University of Edinburgh/NHS Lothian. The sponsors of this study will contribute towards the expenses of the hospital for including you in this study

20. Who has reviewed the study?

This study was given a favourable ethical opinion for conduct in the NHS by the Scotland A Research Ethics Committee. Each hospital participating in the study also reviews the study and must agree to your Doctor taking part

21. Who should I contact?

If you are interested in participating in Opptimum main study or would like further information, please contact:

Name of local Doctor _____

Hospital: _____

Address: _____

_____

_____

Telephone: _____

Email: _____

You will be given a copy of the information sheet and a copy of your signed consent form to keep.

Thank you for or taking time to read this sheet and for considering taking part.