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Thyroid AntiBodies and LEvoThyroxine Study

Participant Information Sheet

Invitation to participate in the TABLET study

You are invited to take part in a research study to find out whether thyroid hormone supplements can help prevent miscarriage. This study is called TABLET (**T**hyroid **A**nti**B**odies and **LE**vo**T**hyroxine Trial) and compares a type of thyroid hormone (levothyroxine) 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 will 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/gynaecologist or the research nurse/midwife for further advice.

PART ONE of this leaflet tells you about the purpose of the TABLET study and what will happen if you take part.

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

PART ONE

What is the purpose of the study?

Recent scientific research has shown that thyroid antibodies are associated with miscarriage. About 1 in 4 or 5 pregnancies end in miscarriage but, the risk approximately doubles if a woman has thyroid antibodies in her blood.. Thyroid antibodies are also associated with premature births. Why thyroid antibodies increase the risk is unclear.

The TABLET study aims to find out if treatment with levothyroxine (a thyroid hormone tablet) can reduce miscarriage and premature births in women with thyroid antibodies .

Why have I been asked to take part?

You have been asked to take part because the blood test that you had showed that you have thyroid antibodies. Your **thyroid hormone** tests were normal – this means that you **do not** have a thyroid illness that requires treatment.

We understand that this might be a difficult time for you and your partner. \As you wish to try for a baby within the next yearwe would like to invite you to take part in this trial. The TABLET trial is looking at the effect of thyroid hormone supplements in pregnancy, so we need to work with couples who will shortly be trying to conceive again.

We aim to recruit 900 women with thyroid antibodies from throughout the country to this study.

Do I have to take part?

You do not have to take part. It is entirely 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 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 your medical care in any way. Whether you take part or not, you will have the same access to support.

If I take part will I have levothyroxine or the placebo treatment?

Neither you nor a doctor can choose which treatment you receive. The decision is made randomly by computer at the TABLET study 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 levothyroxine group or the dummy drug (placebo) group. In addition, neither you nor your gynaecologist/obstetrician or nurse/midwife or GP will know which of the groups you will be in. 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 morning whilst you are trying to get pregnant. If and when you get pregnant, you will be asked to keep taking one capsule every morning until the end of the pregnancy. This is in addition to any other drugs that the doctors looking after you think is appropriate for you during the time you are trying for a baby and during pregnancy.

Will the thyroid hormone supplements help me get pregnant again?

No, there is no evidence to suggest that thyroid hormone supplements will help you conceive..

What happens if I don't get pregnant?

We don't want you to feel pressurised to get pregnant and to know that at any time, you may decide to wait before trying again. We will ask you take the tablets for up to one year. We have chosen to approach more women than is needed to answer the question about miscarriage because we know some will not get pregnant.

What will I have to do?

Pre pregnancy You will be asked to take 1 capsule daily, and give a blood sample at each clinic visit. You will be given a 13 week supply of capsules to begin with. You will be asked to return to the clinic about 3 and 6 months after you start the capsules to have a blood test and to receive another 13 weeks supply. You will have another clinic visit about 9 months after the start and you will receive a final 13 weeks supply of capsules.

During Pregnancy If you become pregnant at any point, you will need to inform your research nurse/midwife and the clinic timetable may then change to fit in around the routine ante-natal clinic visits. You will come for three clinic visits: when you are 6-8 weeks, 16-18 weeks and about 28 weeks of pregnancy. Wherever possible we

will try to fit in with your ante-natal clinic appointments. You will be given further supplies of capsules at each visit.

You may also be asked if some of the blood that is taken can be used for quality control purposes, and possible future research. Any blood used in this way would be anonymised (so your name is not registered with it). Again it is entirely up to you to decide if you want to allow this or not.

Follow-up We will collect information about the outcome of your pregnancy, the number of weeks of pregnancy, and details about you and your baby up until he or she is 4 weeks old. We will not take blood from your baby for the study at any time. We may need to contact you by letter, telephone or e-mail after the baby is born, with your permission.

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

Levothyroxine is taken by millions of pregnant and non-pregnant people worldwide without side effects. We do not expect any particular side-effects for people who take part in the study but we will look out for any problems in case this might happen.

The blood samples given at clinic visits will test if your thyroid hormone levels have become too high or too low. If this happens, you may be told to stop the study treatment and you will be treated appropriately. If you do feel ill in any way at all, you must tell your doctor or the midwife/nurse, who will check to see whether you are having a side effect of the drug.

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

You might not gain any personal benefit. Firstly, we don't know whether you will be taking the thyroid hormone supplement or the dummy drug. Secondly, we hope levothyroxine will help reduce the risk of miscarriage and premature birth, but we cannot be sure in advance whether this is the case – that is the reason for doing this study.

The main benefit from the TABLET study will be that information gained from the study will help improve the options available in the future for women in similar circumstances..

What are the possible risks and disadvantages of taking part?

Levothyroxine is safely used by many millions of people who have low thyroid hormone levels, mainly older people. The risk of too low or too high thyroid hormone levels in women of reproductive age is very low and the very first blood test would have detected the tiny minority of women with non-normal levels. The regular blood tests will monitor the level throughout the study and appropriate care offered if necessary.

There are some classes of drugs that interact with levothyroxine. Please tell your obstetrician if you are, or start taking, any prescription drugs. You will be given a leaflet about interactions, potential side effects and how to take your capsules when you receive each batch.

Taking the blood sample may be a little painful and may result in short-lived bruising.

If you are interested in the TABLET study, 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 TABLET study on an ongoing basis, as well as information from other relevant trials. If thyroid hormone supplements unexpectedly turn out to increase the risk of miscarriage, or cause other problems, this would be detected as soon as possible and the study 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 progress. All information will be kept confidential (see section below).

The reason for the follow-up is that an important aim of the study 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 if you get pregnant or when the baby is born In the unlikely event of you losing the ability to give continued consent during the study. with your permission, we would also like to keep data that we have already collected about you for research purposes.

What if there is a problem?

Whether or not you take part in this project, you would retain the same legal rights as any other patient treated in the National Health Service.

If you are harmed by taking part in this research project, there are no special compensation arrangements. But if you are harmed due to someone's negligence, then you have grounds for a legal action, though you may have to pay for it.

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, you can use the normal National Health Service complaints process : 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, your doctor will send basic information about you and your condition to the TABLET 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 and your treatment will be kept confidential.

If you take part in the study, your relevant medical records may be inspected by authorised individuals from the BCTU. They may also be looked at by regulatory authorities. The purpose of this is to check the study 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 stored for at least 5 years (but ideally not less than 25 years). Arrangements for confidential destruction will then be made.

We aim to conduct a follow-up study, looking at the development of babies born to mothers in the TABLET study. We wish to contact you via your GP when your baby is two years old to ask for your consent to the follow-up study.

What will happen to the results of the research study?

When the results of the TABLET 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 TABLET Study.

Who has organised, reviewed and funded the research?

The TABLET Study is funded by the National Institute for Health Research. The Clinical Trials Unit at the University of Birmingham will collect and analyse the data. The study is sponsored by the University of Birmingham. 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 levothyroxine in pregnant women and women trying to get pregnant in this study.

The doctors involved are not being paid for recruiting women into the study. Women are not paid to take part either, but their help in finding out more about how best to prevent miscarriage 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 TABLET study. Please keep this copy of the TABLET Study Participant Information Sheet. You will also be given a copy of your signed consent form to keep if you decide to participate in the TABLET study.

If you have any questions about the study now or later feel free to ask your specialist or the research midwife or nurse.

Other Useful Contacts

Miscarriage Association; email info@miscarriageassociation.org.uk or telephone helpline 01924 200799 (Mon-Fri, 9am - 4pm)

Website: www.miscarriageassociation.org.uk

Infertility Network UK
Charter House
43 St Leonards Road
Bexhill on Sea
East Sussex TN40 1JA
Tel: 0800 008 7464
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Email: admin@infertilitynetworkuk.com www.infertilitynetworkuk.com

Thank you for taking the time to read this Participant Information Sheet about the TABLET study.