Aspirin versus Placebo in Twin Pregnancies for Preeclampsia Prevention (ASPRE-T)

Patient information leaflet

You are being invited to take part in a research study. Before you decide whether 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 the following information carefully and discuss it with friends, relatives and your GP if you wish. If you have any questions or require any further information please contact the trial co-ordinators at King's College Hospital, the Principal Investigator Prof Kypros Nicolaides.

What is the purpose of the study?

Twin pregnancies have a high risk (about 9%) of developing preeclampsia. This is a medical condition that can happen during pregnancy after 20 weeks and it is characterised by the development of high blood pressure and the presence of protein in the urine and can have serious consequences for the mother and the babies. For the mother, preeclampsia can be associated with serious complications such as liver, kidney and hematological dysfunction (decrease in blood platelets), which can be seen with a laboratory test. Also can cause neurological problems and some symptoms that you can recognise are: headaches, blurry vision, nausea or vomiting. In rare occasions, it can cause stroke and seizures and later in life is related with an increased risk of developing high blood pressure and metabolic disease. For the babies, preeclampsia can cause poor growth, increased risk of stillbirth and premature delivery (being born early), which can also bring other problems for the babies brain and lung development. We are carrying out a study to determine whether taking low-dose aspirin can reduce the risk of preeclampsia and avoid these complications.

Why have I been chosen?

All women over the age of 18 with twin pregnancies attending for their first trimester ultrasound are invited to participate.

Do I have to take part?

It is up to you whether or not to take part in the study. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the care you receive.

What will happen to me if I take part?

Sometimes we do not know which is the best way to treat patients and we need to make comparisons. If you are willing to take part in the aspirin study you will be allocated to receive either aspirin or the inactive comparator (placebo which looks like the real thing but contains no active ingredient). If you are allocated in the placebo group you will not receive a direct benefit from your participation into the trial. You have an equal chance of being allocated into one of the two groups (like the tossing of a coin). We will give you tablets to take once a day until your pregnancy progresses to 36 weeks. Neither you nor we will know if you are taking the real drug or the inactive comparator until the end of the study.

Your routine pregnancy care will include a series of ultrasound scans to monitor the growth and development of your babies. If you agree to take part in the trial the following will happen:

(a) You will sign the consent form; a unique participant study ID will be created for you and we will give you the trial tablets. If you agree we will also let your GP know that you will be taking part in this study. The bottles we will give you includes a small bag, this is called a desiccant which is used to keep the tablets dry, please keep it inside the bottles at all times and do NOT eat.
(b) During four of your visits for a routine scan (around 20, 28, 32 and 36 weeks) we will ask you to bring the trial drug so that we can count the remaining tablets and will also go through a diary you will keep about any side effects or concerns you may have.
(c) During the visits at 20 and 32 weeks we will also ask for your permission to save some of your blood sample. The sample will be processed into plasma and serum and the analysis might include biochemical and hematological tests, proteomics, metabolomics and DNA/RNA analysis. This sample will be stored for future analysis for the prediction of preeclampsia and other pregnancy complications. The samples will be stored in secure fridges in the UK at the Fetal Medicine Research Institute at the Harris Birthright Centre for 10 years and only authorised personnel will have access to the sample
(d) On three occasions (around 16 weeks, 24 weeks and 30 days after the delivery) we will call you to enquire about the progress of your pregnancy, ask you to count the remaining tablets and about any side effects or concerns you may have.
(e) After the end of your pregnancy we will collect data on the outcome of your pregnancy, including the health of your babies until they are discharged (this includes if the babies are admitted to intensive care). We will check your medical records to obtain this information and this is to make sure accurate data on your health and your babies has been recorded. If this information is incomplete, we might contact your GP to get complete data on your pregnancy outcome.

What do I have to do?

You should tell us if you suffer from any illness, or have had an illness in the past. On the basis of this information and the results of your routine scan at 11-13 weeks we will advise you whether you can take part in the study or not. There are no other restrictions as to what you can or cannot do.

What is aspirin?

Aspirin is a drug which is very commonly used to treat headaches and other minor ailments. It is also taken routinely to prevent heart attacks in individuals at high risk of having a heart attack.
(**Note: both the aspirin and the placebo are suitable for Vegetarians, Vegans and Gluten Free).**

Why use aspirin for prevention of preeclampsia?

We have good evidence that in singleton pregnancies use of aspirin can reduce the chances of developing preeclampsia. However, we do not know if aspirin is also beneficial in preventing preeclampsia in twin pregnancies.

What are the side effects of aspirin?

The use of low-dose aspirin is considered safe in pregnancy. Aspirin may cause indigestion and increased bleeding. At high doses aspirin may cause allergic reactions, stomach ache or nausea and may even cause anaemia. For this reason, you should not take more than 2 tablets daily, if you forget to take the tablets one night, just start again the next day. If you think you have a side effect from the treatment please let us know at your next visit. You can also contact the trial co-ordinator if you are concerned.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the PI, Professor Kypros Nicolaides who will do their best to answer your questions (please contact his secretary Eliza Tylki at eliza.tylki@nhs.net, Tel: 020 3299 8256). If you remain unhappy and wish to complain formally, you can contact the local Patient Advice and Liaison Service (PALS) at 020 3299 3601 or email kch-tr.PALS@nhs.net.

Fundación para la Formación e Investigación Sanitaria (FFIS) (the trial lead co- Sponsor) has insurance arrangements for this study. In the unlikely event that you are injured by taking part in this trial, compensation may be available. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against King's College Hospital and the trial lead co-Sponsor (FFIS) but you may have to pay your legal costs.

What will happen to information about me collected during the trial?

We will need to use information from you and your medical records for this research and to ensure your safety. King's College Hospital will collect information from you and your medical records for this research trial in accordance with the lead co- sponsor's instructions. King's College Hospital will keep your name, hospital number and contact details confidential and will not pass this information to the lead co-sponsor. King's College Hospital will use this information, as needed, to contact you about the research trial, make sure that relevant information about the trial is recorded for your care and to check that the research is being done properly. People from the lead co- sponsor and regulatory organisations may look at your medical and research records to check the accuracy of the research trial. The lead co-sponsor will only receive information without any identifying information, your data will have a participant study ID and this is a code, so people who do not need to know who you are will not be able to see your name or contact details (pseudonymised data). The data will be recorded in an electronic data base within secure password- protected hospital computers and only delegated people will have access to this pseudonymised information. The people who analyse the information will not be able to identify you and will not be able to find out your name, hospital number or contact details. King's College Hospital will keep identifiable information about you from this trial for a minimum of 10 years after the trial has finished. Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules.

Fundación para la Formación e Investigación Sanitaria (FFIS) is the lead co- sponsor for this trial based in Spain and has delegated some of their responsibilities as the Sponsor to the Fetal Medicine Foundation (FMF) in the UK. The lead co- sponsor and FMF will be using information from you and your medical records in order to undertake this trial. The lead co- sponsor will act as the data controller for this trial. This means that we are responsible for looking after your information and using it properly. The lead co- sponsor and FMF will keep identifiable information about you for 10 years after the trial has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. You can stop being part of the study at any time, without giving a reason, and all information and samples already collected will be destroyed To safeguard your rights, we will use the minimum personally-identifiable information possible.

If you wish to know more about how we use your information , please contact the FFIS Data Protection Delegate (dpdigs@listas.carm.es) or the FMF delegate (jon.curtissgreen@net). If you agree to take part in this trial, the trial doctor and the study team will send information about you and your progress to the lead co- sponsor and FMF. The information will be processed by the trial team based at the FMF. Your hospital notes may also be looked at by lead co- sponsor and FMF staff if necessary.

What will happen to the results of the study?

Once the study is complete, the results will be published in a medical journal. You will not be identified in any report or publication. The results of the study will also be published at the website of the Fetal Medicine Foundation (https://www.fetalmedicine.org) and If you like, you will be able to find out which treatment group you were in when the study is finished by contacting the trial co-ordinator.

Who is organising and funding the research?

Funding to conduct the trial is provided by The Fetal Medicine Foundation (UK Charity No: 1037116).

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favorable opinion by London – Surrey boarders Research Ethics Committee.

The lead co-Sponsor for the study in this country is Fundación para la Formación e Investigación Sanitaria (FFIS).