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Prevention of preterm birth in twin pregnancies - “Randomised trial of progesterone versus placebo”

Submission date
11/10/2015

Recruitment status
No longer recruiting

Registration date
19/11/2015

Overall study status
Completed

Last Edited
26/01/2021

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
It has been found that the more babies a pregnant mother is carrying, the more likely she is to give-birth early (preterm). Complications for the baby are usually very small, as most preterm births take place after 32 weeks. If the babies are born earlier than this, it can lead to heart, breathing or brain problems. Progesterone is a hormone which is naturally produced in a woman’s body. It plays an important part during pregnancy by helping to nurture the foetus and maintain the womb (uterus) through pregnancy. Studies have shown that progesterone can help to protect against preterm births in women carrying one baby (singleton pregnancy). So far this does not appear to be the case when a woman is carrying twins, however this may be because it is given too late during pregnancy at too low a dose. There are many types of progesterone available, and so the type used may also have an impact on its effectiveness at preventing preterm births. The aim of this study is to find out whether the progesterone containing product Utrogestan can help to prevent preterm births in women carrying twins.

Who can participate?
Women over 18 years of age who are pregnant with twins.

What does the study involve?
Participants are randomly allocated to one of two groups. The first group are asked to insert suppositories (a capsule which is placed in the vagina) containing 300mg progesterone twice a day until 34 weeks gestation (pregnancy) or earlier if the baby is born prematurely. The first group are asked to insert suppositories containing a placebo (dummy) twice a day until 34 weeks gestation (pregnancy) or earlier if the baby is born prematurely. At the end of the study, the amount of babies that are born prematurely are recorded, as well as any complications, such as low birth weight, need for special care or stillbirth.

What are the possible benefits and risks of participating?
Participants may benefit from the potential effect of progesterone in preventing preterm delivery. Not all participants will gain benefit because half of them will receive a placebo drug. Irrespective of which treatment group participants are assigned to, they will benefit from the

close monitoring that they will receive. Participants will not be denied anything they would usually receive as part of routine care by being part of this study. Risks of participating are small, however some patients may experience some mild vaginal discharge or irritation. Previous studies involving progesterone in pregnancy have not reported any side effects. Progesterone is safe for pregnant women and their fetuses throughout pregnancy and is not associated with birth defects.

Where is the study run from?
Hospital Universitario “Virgen de la Arrixaca" (Spain) and six hospitals in the UK

When is the study starting and how long is it expected to run for?
March 2015 to March 2018

Who is funding the study?
Fetal Medicine Foundation (UK)

Who is the main contact?
1. Dr Catalina De Paco (Scientific)
2. Professor Kypros Nicolaides (Scientific)
3. Miss Liona Poon (Scientific)

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2015-005180-16

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Early vaginal progesterone for the preVention of spontaneous prEterm birth iN TwinS: A randomised, placebo controlled, double-blinded trial- EVENTS

Acronym
EVENTS

Study objectives

In twin pregnancies, the use of a vaginal progesterone (urtogestan) started in the first trimester will reduce the chances of having a preterm birth before 34 weeks gestation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Bridge REC, 22/02/2016, ref: 16/LO/0066

Study design
Multi-centre double-blind placebo-controlled randomised trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet.

Health condition(s) or problem(s) studied
Preterm birth

Interventions
All women with a twin pregnancy attending for their routine first trimester scan will be invited to participate in this randomised controlled trial of progesterone versus placebo. Informed and written consent will be sought from those agreeing to participate in the study. Participants are then randomly allocated to the treatment group or the placebo group.

Treatment group: Participants are required to insert a 300mg progesterone suppository twice daily until 34 weeks' gestation or earlier in the event of preterm delivery.

Control Group: Participants are required to insert a 300mg placebo suppository twice daily until 34 weeks' gestation or earlier in the event of preterm delivery.

Follow--up clinical visits for all participants will be carried out at every 2-4 weeks. They will also be followed up by a further telephone interview 30 days after the last dose of medication.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Utrogestan

Primary outcome measure
Incidence of spontaneous delivery before 34 weeks (238 days) of gestation.

Secondary outcome measures
1. The incidence of spontaneous preterm birth <37 weeks (259 days) of gestation
2. Birth weight below the 3rd, 5th and 10th centile
3. Rate of stillbirth or neonatal death due to any cause
4. Major adverse outcomes before discharge from the hospital (intraventricular haemorrhage, respiratory distress syndrome, retinopathy of prematurity, or necrotising entercolitis)
5. Need for neonatal special care (admission to a neonatal intensive care unit, ventilation, phototherapy, treatment for proven or suspected sepsis, or blood transfusion)

Overall study start date
01/03/2015

Completion date
01/12/2019

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. Dichorionic diamniotic (DCDA) or monochorionic diamniotic (MCDA) twin pregnancies;
3. Live fetuses at 11-13 weeks of gestation;
4. English or Spanish speaking (otherwise interpreters will be used)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
1,180

Total final enrolment
1194

Key exclusion criteria

1. Pregnancies complicated by major fetal abnormality identified at the 11-13 weeks assessment, including nuchal translucency thickness >3.5 mm
2. In MCDA twin pregnancies there are early signs of twin-to-twin transfusion syndrome (TTTS) (20% discordance in crown-rump length [CRL] and/or nuchal translucency [NT])
3. Women who are unconscious or severely ill, those with learning difficulties, or serious mental illness
4. Hypersensitivity to progesterone
5. Concurrent participation in another drug trial or at any time within the previous 28 days
6. Any other reason the clinical investigators think will prevent the potential participant from complying with the trial protocol

Date of first enrolment
02/05/2017

Date of final enrolment
18/04/2019

Locations

Countries of recruitment
England

Spain

United Kingdom

Study participating centre
Hospital Universitario “Virgen de la Arrixaca"
Murcia
Spain
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Study participating centre
King's College Hospital London
Denmark Hill
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Study participating centre
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Study participating centre
North Middlesex Hospital
Sterling Way
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Sponsor information

Organisation
Foundation for Health Education & Research (Fundación para la Formación e Investigación Sanitaria)

Sponsor details

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Murcia
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30003

Sponsor type
Not defined

ROR
https://ror.org/05m5has32

Funder(s)

Funder type
Charity

Funder Name
Fetal Medicine Foundation

Results and Publications

Publication and dissemination plan
Intention to publish the trial outcomes in peer reviewed journals. Results will also be made available at www.fetalmedicine.org/publications

Intention to publish date
01/01/2020

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2021	26/01/2021	Yes	No
HRA research summary			28/06/2023	No	No