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Progesterone in recurrent miscarriages (PROMISE) study

Submission date
10/03/2009

Recruitment status
No longer recruiting

Registration date
17/03/2009

Overall study status
Completed

Last Edited
31/05/2016

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
This study was undertaken to test whether giving the hormone progesterone to pregnant women with a history of repeated unexplained early pregnancy losses could increase the number of pregnancies leading to live births after at least 24 weeks of gestation.

Who can participate?
Women aged 18-39 with unexplained recurrent miscarriages (three or more consecutive or non-consecutive first trimester miscarriages). A pregnancy loss is considered to be unexplained if conditions known to increase the risk of miscarriage are absent.

What does the study involve?
Participants were randomly allocated to one of two groups: one group received progesterone twice daily as vaginal pessaries and the other group received a placebo (dummy) with an identical appearance, from soon after a positive urinary pregnancy test, and no later than 6 weeks of pregnancy, until 12 completed weeks of pregnancy (or earlier if the pregnancy ended before 12 weeks).

What are the possible benefits and risks of participating?
There is substantial evidence from IVF practice that progesterone supplementation is safe to the mother and fetus at the proposed dose. Moreover, recent studies of vaginal progesterone in the context of prevention of preterm birth have not shown any evidence of short-term safety concerns in the participants.

Where is the study run from?
45 hospitals in the UK and the Netherlands

When is the study starting and how long is it expected to run for?
From May 2009 to September 2014

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
1. Dr Arri Coomarasamy (a.coomarasamy@bham.ac.uk)
2. Dr Rajendra Rai (r.rai@imperial.ac.uk)

Study website
http://www.medscinet.net/promise

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 08/38/01

Study information

Scientific Title
First trimester progesterone therapy in women with a history of unexplained recurrent miscarriages: a randomised double-blind placebo-controlled multi-centre trial (The PROMISE [PROgesterone in recurrent MIScarriagE] Trial)

Acronym
PROMISE

Study objectives
1. In women with unexplained recurrent miscarriages, progesterone (400 mg pessaries, twice daily), started soon as possible after a positive pregnancy test (and no later than 6 weeks gestation) and continued to 12 weeks of gestation, compared to placebo, increases live births beyond 24 completed weeks by at least 10% (principal objective)
2. Progesterone improves secondary outcomes such as gestation at delivery, on-going pregnancy at 12 weeks, survival at 28 days of neonatal life
3. Progesterone, compared to placebo, does not incur substantial adverse effects to the mother or the neonate
4 Explore differential or subgroup effects of progesterone in prognostic subgroups
5. Perform an economic evaluation for cost-effectiveness

More details can be found at http://www.nets.nihr.ac.uk/projects/hta/083801
Protocol can be found at http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0018/52911/PRO-08-38-01.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
REC: West Midlands Research Ethics Committee, 19/10/2009, ref: 09/H1208/44

Study design
Randomised double-blind placebo-controlled multi-centre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Unexplained recurrent miscarriages

Interventions
Intervention group: Progesterone pessaries (400 mg twice daily) started soon as possible after a positive pregnancy test (and no later than 6 weeks gestation) and continued to 12 weeks of gestation

Control group: Placebo

Total duration of follow-up per participant: 42 weeks

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Live births beyond 24 weeks

Secondary outcome measures
1. Gestation at delivery
2. Clinical pregnancy at 6-8 weeks
3. Ongoing pregnancy at 12 weeks (range 11-13 weeks)
4. Miscarriage rate
5. Survival at 28 days of neonatal life
6. Congenital abnormalities with specific examination for genital anomalies
7. Adverse events

Overall study start date
01/05/2009

Completion date
01/09/2014

Eligibility

Key inclusion criteria

1. Women with unexplained recurrent miscarriages (3 or more consecutive first trimester miscarriages)
2. Age 18-39 years at randomisation (likelihood of miscarriages due to chromosomal aberrations is higher in older women; such miscarriages are unlikely to be prevented by progesterone therapy)
3. Spontaneous conception (as confirmed by urinary pregnancy tests)
4. Willing and able to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
39 Years

Sex
Female

Target number of participants
790

Key exclusion criteria
1. Inability to conceive spontaneously within 1 year of recruitment
2. Antiphospholipid syndrome (lupus anticoagulant and/or anticardiolipin antibodies [IgG or IgM]); other recognised thrombophilic conditions (testing according to usual clinic practice)
3. Intrauterine abnormalities (as assessed by ultrasound, hysterosonography, hysterosalpingogram, or hysteroscopy)
4. Fibroids distorting uterine cavity
5. Abnormal parental karyotype
6. Other identifiable causes of recurrent miscarriages (tests initiated only if clinically indicated) e. g., diabetes, thyroid disease and systemic lupus erythematosus (SLE)

Date of first enrolment
01/06/2010

Date of final enrolment
01/10/2013

Locations

Countries of recruitment
Netherlands

United Kingdom

Study participating centre
45 hospitals in the UK and the Netherlands
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Sponsor information

Organisation
Imperial College London (UK)

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Sponsor type
University/education

Website
http://www.imperial.ac.uk

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Publication in the UK NIHR HTA library is anticipated before the end of 2015. Other publications may be produced but are not yet confirmed.

Intention to publish date
01/11/2015

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	26/11/2015		Yes	No
Results article	results	01/05/2016		Yes	No
HRA research summary			28/06/2023	No	No