

Progesterone in recurrent miscarriages (PROMISE) study

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| Submission date 10/03/2009 | Recruitment status No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol |
| Registration date 17/03/2009 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 31/05/2016 | Condition category Pregnancy and Childbirth | <input type="checkbox"/> 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?

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Contact information

Type(s)

Scientific

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Additional identifiers

Protocol serial number

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

Study type(s)

Treatment

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(s)

Live births beyond 24 weeks

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

39 years

Sex

Female

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**

United Kingdom

Netherlands

Study participating centre

45 hospitals in the UK and the Netherlands

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Sponsor information**Organisation**

Imperial College London (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, Health Technology Assessment (HTA), HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

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 |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |