PRISM: Progesterone in spontaneous miscarriage

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
11/02/2015		☐ Protocol		
Registration date	Overall study status Completed	Statistical analysis plan		
11/02/2015		[X] Results		
Last Edited	Condition category	[] Individual participant data		
02/07/2020	Pregnancy and Childbirth			

Plain English summary of protocol

Background and study aims

One in five pregnancies miscarry, and the loss of an unborn baby has the potential to cause both physical harm and psychological distress. A recently launched NICE guideline has urged that a large and robust randomised controlled clinical trial should be done to clarify whether progesterone treatment for women with bleeding in early pregnancy reduces the risk of miscarriage.

Who can participate?

Women between the ages of 18-39 who have experienced bleeding during the last 4 days in early pregnancy (up to 12 weeks).

What does the study involve?

Participants are randomly allocated into one of two groups. Those in group 1 are given progesterone capsules to place into their vagina twice a day to up to 16 weeks of pregnancy. Those in group 2 are given placebo capsules to be administered in the same way. The main outcome of the study is live birth beyond 34 weeks of pregnancy. A number of other key outcome measures, including gestation at birth, miscarriage rates and the condition of the baby at 28 days of life, are also collected and analysed and we gather resource-use outcomes to perform a health economic evaluation.

What are the possible benefits and risks of participating?

We do not know whether each participant will benefit personally from taking part in this study, but the knowledge gained thanks to their help will inform future treatment and potentially lead to improved antenatal care and pregnancy outcomes for women in the future. Previous studies using progesterone treatment during pregnancy have found very little evidence of risks for the mother or the baby. However, some women may experience swollen hands or feet, bloating, headache, sleeplessness, diarrhoea or jaundice.

Where is the study run from? 48 NHS hospitals in the UK

When is the study starting and how long is it expected to run for? October 2014 to June 2018

Who is funding the study? National Institute for Health Research (UK)

Who is the main contact? Professor Arri Coomarasamy

Contact information

Type(s)

Scientific

Contact name

Dr Adam Devall

Contact details

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B15 2TT

Additional identifiers

EudraCT/CTIS number 2014-002348-42

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers 18314

Study information

Scientific Title

Effectiveness of progesterone to prevent miscarriage in women with early pregnancy bleeding: A randomised placebo-controlled trial (PRISM Trial: PRogesterone In Spontaneous Miscarriage Trial)

Acronym

PRISM

Study objectives

The aim of this trial is to clarify the evidence that progesterone treatment for women with bleeding in early pregnancy can reduce the risk of miscarriage.

Ethics approval required

Old ethics approval format

Ethics approval(s)

NRES Committee South Central – Oxford C, 26/11/2014, ref: 14-SC-1345

Study design

Randomised; Interventional; Design type: Not specified, Prevention

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Community

Study type(s)

Treatment

Participant information sheet

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

Health condition(s) or problem(s) studied

Topic: Reproductive health and childbirth; Subtopic: Reproductive Health and Childb (all Subtopics); Disease: Reproductive Health & Childbirth

Interventions

- 1. Placebo: The placebo will be a vaginal capsule, encapsulated in the same form as the IMP, and identical in colour, shape and weight
- 2. Progesterone: The Investigational Medicinal Product (IMP) is progesterone at a dose of 400mg to be taken as vaginal pessaries twice daily from confirmation of an intrauterine gestation sac visible on ultrasonography until 16 completed weeks of pregnancy or until miscarriage is confirmed

Intervention Type

Drug

Drug/device/biological/vaccine name(s)

Progesterone

Primary outcome measure

Live birth beyond 34 completed weeks of gestation is assessed using medical record review at pregnancy end.

Secondary outcome measures

Secondary outcome measures as of 01/02/2017:

- 1. Time from conception to pregnancy end (any reason) is assessed using medical record review at pregnancy end. Conception date will be estimated using the patient's booking scan if available or, if not, the date of last menstrual period or, failing that, the date from the ultrasound scan.
- 2. Ongoing pregnancy at 12 weeks (range 11 to 14 weeks) of gestation is assessed using medical record review at 11-14 weeks gestation
- 3. Miscarriage rate (defined as delivery before 24 weeks of gestation) is assessed using medical record review at pregnancy end
- 4. Other pregnancy end outcomes: live birth <34 weeks, ectopic pregnancy, termination, stillbirth, molar pregnancy, resolved pregnancy of unknown location (PUL), failed PUL, twin live births, gestational age at miscarriage is assessed using medical record review at pregnancy end 5. Where live birth ≥24 weeks: time from conception to delivery (gestational age), gestational age <28/<32/<37 weeks, mode of delivery (unassisted vaginal, instrumental vaginal, elective c-section, emergency c-section, vaginal breech delivery, other), birth weight, arterial and venous cord pH, APGAR scores, base excess is assessed using medical record review at pregnancy end 6. Antenatal complications: pregnancy-induced hypertension, pre-eclampsia, obstetric cholestasis, cervical cerclarge, preterm (<37 weeks) pre-labour rupture of membranes, gestational diabetes (other complications will be tabulated but not formally analysed) (medical record review)
- 7. Intrapartum complications: chorioamnionitis, intrauterine growth restriction (IUGR), macrosomia (other complications will be tabulated but not formally analysed) is assessed using medical record review at pregnancy end
- 8. Post-partum complications: haemorrhage (other complications will be tabulated but not formally analysed) is assessed using medical record review at pregnancy end
- 9. Maternal complications: admission to high dependency unit (HDU), admission to intensive therapy unit (ITU), (other complications will be tabulated but not formally analysed) is assessed using medical record review up to 28 days after pregnancy end
- 10. Neonatal complications: discharge to hospital, early infection, retinopathy of prematurity, necrotising enterocolitis, intraventricular haemorrhage, congenital and chromosomal abnormalities, respiratory distress syndrome, ventilation or oxygen support (other complications will be tabulated but not formally analysed is assessed using medical record review up to 28 days after live birth
- 11. Survival at 28 days of neonatal life is assessed using medical record review up to 28 days after live birth
- 12. Maternal adverse events (tabulated but not formally analysed) is assessed using medical record review throughout pregnancy and up to 28 days of neonatal life
- 13. Serious adverse events are assessed using medical record review throughout pregnancy and up to 28 days of neonatal life

Original secondary outcome measures:

- 1. Adverse events; Timepoint(s): Throughout pregnancy and up to 28 days of neonatal life
- 2. Antenatal complications; Timepoint(s): Until pregnancy end
- 3. APGAR score; Timepoint(s): Pregnancy end beyond 24 weeks
- 4. Arterial cord pH; Timepoint(s): Pregnancy end beyond 24 weeks
- 5. Birthweight; Timepoint(s): Pregnancy end beyond 24 weeks
- 6. Chromosomal and congenital abnormalities; Timepoint(s): Pregnancy end
- 7. Gestation at delivery; Timepoint(s): Pregnancy end
- 8. Miscarriage; Timepoint(s): Up to 24 weeks of gestation
- 9. Mode of delivery; Timepoint(s): Pregnancy end beyond 24 weeks
- 10. Neonatal complications; Timepoint(s): Live birth
- 11. Neonatal survival; Timepoint(s): 28 days of neonatal life

- 12. Ongoing pregnancy at 12 weeks of gestation; Timepoint(s): 11-13 weeks of gestation
- 13. Requirements for resuscitation; Timepoint(s): Pregnancy end beyond 24 weeks
- 14. Resource use; Timepoint(s): Throughout pregnancy and up to 28 days of neonatal life
- 15. Surfactant use; Timepoint(s): Live birth
- 16. Venous cord pH; Timepoint(s): Pregnancy end beyond 24 weeks
- 17. Ventilation support; Timepoint(s): Live birth

Overall study start date

01/10/2014

Completion date

30/06/2018

Eligibility

Key inclusion criteria

Correct as of 01/02/2017

- 1. Women presenting with with early pregnancy vaginal bleeding that has occurred within the last 4 days and is in the first 12 weeks of pregnancy
- 2. Upper Age Limit 39 years
- 3. Lower Age Limit 18 years

Previous inclusion criterion:

1. Women presenting with vaginal bleeding in the first 12 weeks of pregnancy with an intrauterine gestation sac visible on ultrasonography

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Female

Target number of participants

Planned Sample Size: 4150; UK Sample Size: 4150

Total final enrolment

4153

Key exclusion criteria

- 1. Women of age less than 18 years or more than 40
- 2. Women with life-threatening bleeding
- 3. Women already taking progesterone supplementation therapy
- 4. Women with contraindications to progesterone use

Date of first enrolment 01/03/2015

Date of final enrolment 28/07/2017

Locations

Countries of recruitment

England

Scotland

United Kingdom

Study participating centre Birmingham Women's Hospital Metchley Park Road Edgbaston Birmingham

United Kingdom B15 2TG

Study participating centre Queen Charlotte's and Chelsea Hospital London **United Kingdom** W12 0HS

Study participating centre Royal Infirmary of Edinburgh Edinburgh United Kingdom

EH16 4SA

Study participating centre Liverpool Women's Hospital Liverpool United Kingdom **L87SS**

Study participating centre Birmingham Heartlands Hospital Birmingham United Kingdom B9 5SS

Study participating centre
University College London Hospital
London
United Kingdom
NW1 2BU

Study participating centre Chelsea and Westminster Hospital London United Kingdom SW15 2QJ

Study participating centre St Michael's University Hospital Bristol United Kingdom BS2 8UG

Study participating centre Queen's Medical Centre Nottingham United Kingdom NG7 2UH

Study participating centre Sunderland Royal Hospital Sunderland United Kingdom SR4 7TP

Study participating centre Princess Royal HospitalGlasgow

Study participating centre
University Hospital Coventry
Coventry
United Kingdom
CV2 2DX

Sponsor information

Organisation

University of Birmingham

Sponsor details

Edgbaston Birmingham England United Kingdom B15 2TT

Sponsor type

University/education

ROR

https://ror.org/03angcq70

Funder(s)

Funder type

Government

Funder Name

National Institute for Health Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

A meeting will be held after the end of the study to allow discussion of the main results among the collaborators prior to publication in an open access journal.

Intention to publish date

30/06/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	09/05/2019	09/05/2019	Yes	No
Other publications	cost-effectiveness analysis	01/05/2020		Yes	No
Results article	results	01/06/2020	02/07/2020	Yes	No