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First Trimester Aspirin Trial

Submission date
28/10/2010

Recruitment status
No longer recruiting

Registration date
12/01/2011

Overall study status
Completed

Last Edited
24/08/2017

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
The placenta (afterbirth) is responsible for providing food and oxygen to the fetus. When there is a problem with the function of the placenta the fetus may not grow well and the mother can develop high blood pressure (pre-eclampsia). Placental problems affect about 10% of pregnancies. The consequences are usually minor but occasionally they can be serious both for the mother and the baby. On the basis of the findings of our tests (blood flow through the uterine arteries, blood pressure, and blood levels of proteins produced by the placenta), we can determine whether a patient is at increased risk of developing pre-eclampsia. The aim of this study to determine giving these patients a low dose of aspirin reduces their risk of pre-eclampsia.

Who can participate?
Pregnant women aged 18 or over who are at a high risk of developing pre-eclampsia

What does the study involve?
Participants are randomly allocated to take either aspirin or a placebo (dummy drug) once per night until 36 weeks' gestation or when signs of labour commence. All participants are followed up until the last patient has delivered.

What are the possible benefits and risks of participating?
It is not known if there is a direct benefit to a participant's current pregnancy. The participant is in greater regular contact with the clinical team during pregnancy than is routine and the information gained from the study may help the participant and/or other women in the future who are at high risk from developing preeclampsia. The use of low-dose aspirin appears to be safe in pregnancy.

Where is the study run from?
King's College Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2014 to November 2016

Who is funding the study?
European Commission Research: The Seventh Framework Programme (FP7)

Who is the main contact?
Prof Kypros Nicolaides

Study website
http://www.aspre.eu

Contact information

Type(s)
Scientific

Contact name
Prof Kypros Nicolaides

Contact details
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Additional identifiers

EudraCT/CTIS number
2013-003778-29

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
62340803

Study information

Scientific Title
Combined multi-marker screening and randomised patient treatment with ASpirin for evidence-based PRE-eclampsia prevention

Acronym
ASPRE

Study objectives
To examine if the prophylactic use of low-dose aspirin from the first-trimester of pregnancy in women at increased risk for preeclampsia can reduce the incidence and severity of the disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Fulham, 12/11/2013, ref: 13/LO/1479

Study design
Double-blind randomised controlled 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 to request a patient information sheet

Health condition(s) or problem(s) studied
Pre-eclampsia

Interventions
Current interventions as of 16/04/2014:
Randomised participants will be advised to start 150 mg of aspirin or placebo once per night within 24 hours of randomisation until 36 weeks' gestation or when signs of labour commence. The maximum duration for aspirin or placebo intake will be 180 days.

Interventions from 12/03/2013 to 15/04/2014:
Aspirin 150 mg daily versus placebo. The total duration of treatment is 5 months (from 12 weeks' gestation to 34 weeks) and follow-up for all arms will be up to the last randomised patient has delivered.

Original interventions until 12/03/2013:
Aspirin 75 mg daily versus placebo. The total duration of treatment is 6 months (from 12 weeks gestation to 36 weeks) and follow-up for all arms will be up to the last randomised patient has delivered.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)

Aspirin

Primary outcome measure

Current primary outcome measures as of 12/03/2013:
Development of pre-eclampsia, requiring delivery before 37 weeks' gestation

Previous primary outcome measures until 12/03/2013:
Development of pre-eclampsia, measures will be obtained at the end of the pregnancy.

Secondary outcome measures

Current secondary outcome measures as of 21/04/2016:
1. To determine the effect of low-dose aspirin on adverse outcome of pregnancy at <37 weeks
1.1. Pre-eclampsia (PE) requiring delivery at <37 weeks
1.2. Small for gestational age (SGA) (<5th percentile) requiring delivery at <37 weeks
1.3. Miscarriage or stillbirth at <37 weeks
1.4. Placental abruption (clinically or on placental examination) at <37 weeks
1.5. Composite of any of the above
2. To determine the effect of low-dose aspirin on adverse outcome of pregnancy at <34 weeks
2.1. PE requiring delivery at <34 weeks
2.2. SGA (<5th percentile) requiring delivery at <34 weeks
2.3. Miscarriage or stillbirth at <34 weeks
2.4. Placental abruption (clinically or on placental examination) at <34 weeks
2.5. Composite of any of the above
3. To determine the effect of low-dose aspirin on adverse outcome of pregnancy at >37 weeks
3.1. PE requiring delivery at >37 weeks
3.2. SGA (<5th percentile) requiring delivery at >37 weeks
3.3. Miscarriage or stillbirth at >37 weeks
3.4. Placental abruption (clinically or on placental examination) at >37 weeks
3.5. Composite of any of the above
4. To determine the effect of low-dose aspirin on neonatal mortality and morbidity
4.1. Neonatal intensive care unit admission
4.2. Intraventricular haemorrhage (IVH) grade II or above - defined as bleeding into the ventricles
4.2.1. Grade II (moderate) – IVH occupies <50% of the lateral ventricle volume
4.2.2. Grade III (severe) – IVH occupies >50% of the lateral ventricle volume
4.2.3. Grade IV (severe) – haemorrhagic infarction in periventricular white matter ipsilateral to a large IVH
4.3. Ventilation - defined as need of positive pressure (continuous positive airway pressure [CPAP] or nasal continuous positive airway pressure [NCPAP]) or intubation
4.4. Neonatal sepsis - confirmed bacteraemia in cultures
4.5. Anaemia – defined as low haemoglobin and/or haematocrit requiring blood transfusion
4.6. Respiratory distress syndrome - defined as need of surfactant and ventilation as a result of prematurity
4.7. Necrotising enterocolitis (NEC) requiring surgical intervention. NEC is defined by a combination of clinical, radiological and laboratory features:
4.7.1. Systemic signs - apnoea, bradycardia, temperature instability, hypotension
4.7.2. Intestinal signs - abdominal distension, gastric residuals, bloody stools, absent bowel sounds, abdominal tenderness, peritonitis
4.7.3. Radiological signs - pneumatosis intestinalis or portal venous air, pneumoperitoneum
4.7.4. Laboratory changes - metabolic and or respiratory acidosis, thrombocytopaenia, DIC
4.8. Composite of any of the above
5. To determine the effect of low-dose aspirin on the incidence of neonatal birthweight below

the 3rd, 5th and 10th centile
5.1. Birthweight will be recorded in the participants' medical notes and birthweight percentile for gestational age at delivery is calculated using a normal range derived from our population
6. To determine the effect of low-dose aspirin on the incidence of stillbirth or neonatal death
6.1. Due to any cause
6.2. Ascribed to PE or fetal growth restriction (FGR)
6.3. In association with maternal or neonatal bleeding
7. To determine the effect of low-dose aspirin on the incidence of spontaneous preterm delivery at <34 weeks and <37 weeks
7.1. Spontaneous delivery at <34 weeks (early preterm) and at <37 weeks (total preterm) includes those with spontaneous onset of labour and those with preterm pre-labour rupture of membranes

Secondary outcome measures from 12/03/2013 to 21/04/2016:
1. Development of early onset pre-eclampsia requiring delivery before 34 weeks' gestation and pre-eclampsia at any gestation
2. Birthweight below the 3rd, 5th and 10th centile
3. Stillbirth or neonatal death due to any cause
4. Stillbirth or neonatal death ascribed to pre-eclampsia or fetal growth restriction
5. Stillbirth or neonatal death in association with maternal or neonatal bleeding
6. Rate of neonatal intensive care unit admission
7. Composite measure of neonatal mortality and morbidity
8. Placental abruption (clinically or on placental examination)
9. Spontaneous preterm delivery <34 weeks and <37 weeks
Measures will be obtained at the end of the pregnancy.

Previous secondary outcome measures until 12/03/2013:
1. Development of pre-eclampsia according to gestation at delivery: early (less than 34 weeks), intermediate (34 - 37 weeks) and late-PE (greater than 37 weeks)
2. Birthweigth below the 3rd, 5th and 10th centile
3. Stillbirth or neonatal death due to any cause
4. Stillbirth or neonatal death ascribed to pre-eclampsia or IUGR
5. Stillbirth or neonatal death ascribed to maternal or neonatal bleeding
6. Rate of neonatal intensive care unit admission
7. Placental abruption (clinically or on placental examination)
Measures will be obtained at the end of the pregnancy.

Overall study start date
02/01/2014

Completion date
03/11/2016

Eligibility

Key inclusion criteria
Current inclusion criteria as of 12/03/2013:
1. Aged 18 years or over
2. Singleton pregnancies
3. Live fetus at 11-13 weeks of gestation
4. High-risk for preterm pre-eclampsia will be defined at 11-13 weeks by the algorithm

combining maternal history and characteristics, biophysical findings (mean arterial pressure and uterine artery Dopplers) and biochemical factors (pregnancy associated plasma protein-A [PAPP-A] and placental growth factor [PlGF]).

Previous inclusion criteria until 12/03/2013:
All singleton pregnancies with a live foetus at 11+0 - 13+6 weeks of gestation.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
1760

Key exclusion criteria
Current exclusion criteria as of 28/04/2014:
1. Multiple pregnancies
2. Pregnancies complicated by major fetal abnormality identified at the 11-13 weeks assessment
3. Women who are unconscious or severely ill, those with learning difficulties, and serious mental illness
4. Bleeding disorders such as Von Willebrands disease
5. Peptic ulceration
6. Hypersensitivity to aspirin or already on long term non-steroidal anti-inflammatory medication
7. Age < 18 years
8. Women taking low-dose aspirin regularly
9. Concurrent participation in another drug trial or at any time within the previous 28 days
10. Any other reason the clinical investigators think will prevent the potential participant from complying with the trial protocol

Exclusion criteria from 12/03/2013 to 28/04/2014:
1. Multiple pregnancies
2. Pregnancies complicated by major fetal abnormality identified at the 11-13 weeks assessment
3. Women who are unconscious or severely ill, those with learning difficulties, and serious mental illness
4. Bleeding disorders such as Von Willebrands disease
5. Peptic ulceration
6. Hypersensitivity to aspirin or already on long term non-steroidal anti-inflammatory medication
7. Age < 18 years

Original exclusion criteria until 12/03/2013:
1. Major foetal abnormalities identified at the 11+0 - 13+6 weeks assessment
2. Women who are unconscious or severely ill
3. Learning difficulties

4. Serious mental illness
5. Women with bleeding disorders
6. Peptic ulceration
7. Hypersensitivity to aspirin
8. Under the age of 18 years

Date of first enrolment
23/04/2014

Date of final enrolment
14/04/2016

Locations

Countries of recruitment
Belgium

England

Greece

Israel

Italy

Spain

United Kingdom

Study participating centre
King's College Hospital
London
United Kingdom
SE5 9RS

Study participating centre
Hospital Universitario Virgen de la Arrixaca
Murcia
Spain
-

Study participating centre

North Middlesex University Hospital
London
United Kingdom
-

Study participating centre
University Hospital Lewisham
London
United Kingdom
-

Study participating centre
Medway Maritime Hospital
Gillingham
United Kingdom
-

Study participating centre
Southend University Hospital
Westcliff-on-Sea
United Kingdom
-

Study participating centre
Homerton University Hospital
London
United Kingdom
-

Study participating centre
CHU Brugmann
Brussels
Belgium
-

Study participating centre

Hospiten Sur
Tenerife
Spain
-

Study participating centre
Attikon University Hospital
Athens
Greece
-

Study participating centre
Hospital Universitario San Cecilio
Granada
Spain
-

Study participating centre
Ospedale Maggiore Policlinico
Milan
Italy
-

Study participating centre
Rabin Medical Center
Petah Tikva
Israel
-

Sponsor information

Organisation
University College London (UK)

Sponsor details
c/o Susan Tebbs
Gower Street

London
United Kingdom
WC1E 6BT

Sponsor type
Government

Website
http://www.ucl.ac.uk/cctu

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research council

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal during 2017.

Intention to publish date
03/11/2017

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	28/06/2016		Yes	No
Results article	results	17/08/2017		Yes	No
HRA research summary			28/06/2023	No	No