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Pravastatin for Pregnancies complicated by Ischemical Placental Disease

Submission date	Recruitment status	[X] Prospectively registered
19/02/2018	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
17/03/2018	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/03/2018	Pregnancy and Childbirth	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Ischemic placental disease (IPD) is a term for diseases caused by the failure to deliver enough nutrients and oxygen to the placenta during pregnancy. IPD includes preeclampsia (maternal high blood pressure) and intrauterine growth restriction (IUGR, where the unborn baby is smaller than it should be). The only treatment for these complications is delivery, and medication only treats the symptoms. Statins may prove useful in the treatment of IPD. The aim of this study is to investigate the effect of pravastatin on pregnant women with IPD.

Who can participate?
Pregnant women with preeclampsia and/or IUGR

What does the study involve?
Participants are treated with pravastatin and routine examinations are performed while they remain hospitalised. Blood samples are taken every 3 days until delivery. Blood pressure is measured using an automated electronic device daily. A 24h urine sample is collected at admission. An ultrasound is performed weekly. Pregnancy prolongation interval from diagnosis to delivery and the number of fetal/neonatal deaths are compared with a sample of women hospitalised during the previous 5 years who were not treated with pravastatin.

What are the possible benefits and risks of participating?
Statins may prove useful in the treatment of IPD, and participants may benefit from improved pregnancy outcomes. Regarding risks, the effects of pravastatin on pregnancy are still unknown, but recent studies have reported that statins like pravastatin do not cross the placenta and do not affect the baby's development.

Where is the study run from?
Aristotle University of Thessaloniki (Greece)

When is the study starting and how long is it expected to run for?
June 2017 to December 2020

Who is funding the study?
Aristotle University of Thessaloniki (Greece)

Who is the main contact?
Dr Stamatios Petousis

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1276

Study information

Scientific Title
Effect of PRAvastatin in Pregnancies complicated by Ischemical Placental Disease: prospective observational study

Acronym
E PRA PIPD

Study objectives
The aim of this study is to investigate the effect of pravastatin administration in pregnant women with placental insufficiency and specifically on the latency period of pregnancy, on the levels of endothelial factors in the blood and also on maternal and neonatal morbidity and mortality.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Longitudinal observational study

Primary study design
Observational

Secondary study design
Longitudinal study

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
Preeclampsia (PE), intrauterine growth restriction (IUGR) and placental abruption

Interventions
Following the diagnosis of placental insufficiency, either at the outpatient clinic level or following a referral from a private practice to the high-risk pregnancy clinic and confirmation by the head of the Maternal Fetal medicine unit, Prof Mamopoulos, the patient will be offered participation in the study. In case of acceptance, 20 mg of pravastatin will be administered orally. The patient will remain hospitalised and routine examinations including clinical assessment, laboratory tests and ultrasound scans will be performed according to the clinic's protocols. For the purposes of the study, peripheral blood samples will be taken every 3 days until delivery and these will be centrifuged and stored in a freezer at -80o Celsius.

For every pregnant woman enrolled in the study, a full gynaecologic, obstetric, personal and family history will be recorded. Furthermore, all participants will be examined as follows:
1. Blood pressure using an automated electronic device (daily)
2. Protein in 24h collected urine (at admission)
3. Blood tests every 3 days (full blood count, urea, creatinine, tranaminases, glucose, K,Na, INR, fibrinogen, PT, aPTT) and urine protein
4. Ultrasound performed weekly, at which the estimated fetal weight, umbilical artery PI, middle cerebral artery PI, PI in the ductus venosus, uterine arteries PI and the max vertical pocket of amniotic fluid will be recorded

Intervention Type

Primary outcome measure
1. Pregnancy prolongation interval from diagnosis to delivery is estimated between day of entrance in the trial (which is the first day of pravastatin administration) and day of pregnancy delivery

2. Intrauterine or neonatal death in fetuses/neonates is measured using medical records from the day of entrance in the trial (which is the first day of pravastatin administration) until the 28th day of neonatal life

Secondary outcome measures
1. MAP (SAP and DAP) is measured using blood pressure measurement at 1 week
2. PI values of the Umbilical, MCA, DV uterine arteries are measured using obstetrical ultrasound (brandname GE Voluson S10) twice a week, namely the 3rd and 7th day of every consecutive week (days 0,3,7,10, 14…) until the day of pregnancy delivery
3. Endothelial parameters values, especially endogline and sflt-1, measured using Western blot between the start of therapy and serial measurements until delivery as previously mentioned
4. Neonatal morbidity parameters, more specifically respiratory distress syndrome, cerebral bleeding, sepsis and necrotic enterocolitis, are measured using neonatal medical records during Neonatal Intensive Care Unit (NICU) hospitalization from the day of NICU admission until NICU dischargement

Overall study start date
01/06/2017

Completion date
31/12/2020

Eligibility

Key inclusion criteria
1. Pregnant women with PE and/or IUGR diagnosed between 20 and 34 gestational weeks, irrespective of maternal age.
2. PE will be defined as a newly onset hypertension in pregnancy (SAP > 140 mm Hg or DAP > 90 mm Hg) and significant proteinuria (>300mg/24h)
3. IUGR is defined as an estimated fetal weight <10th percentile with associated findings of placental insufficiency as a high resistance in the uterine arteries or in the umbilical artery (Pulsatility Index>95th percentile) or reduced amniotic fluid (maximum vertical pocket < 2 cm)

The control group:
1. Historical sample of women that were hospitalised during the 5 previous years in the Maternal fetal medicine unit of the 3rd Obstetrics and Gynecology University clinic
2. Pravastatin not used in treating the disease
3. Controlled for maternal age and the estimated fetal weight percentile.

Participant type(s)
Patient

Age group
Other

Sex
Female

Target number of participants

Based on the prolongation interval as the main outcome and considering previous clinical data where the average interval was 21 + 9 days, and accepting a 7 days interval as clinicoally significant, for a statistical significance of 0.05 and statistical pwer of 90%, 35 women per group are needed (70 cases overall).

Key exclusion criteria
1. Pre-existing hypertension
2. Renal
3. Liver or connective tissue disease
4. Uterine malformations
5. Twin pregnancy
6. Fetal chromosomal abnormalities

Date of first enrolment
01/04/2018

Date of final enrolment
31/03/2019

Locations

Countries of recruitment
Greece

Study participating centre
Aristotle University of Thessaloniki, Greece
3rd Department of Obstetrics and Gynaecology
Medical School
Faculty of Health Sciences
Konstantinoupoleos 49
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Sponsor information

Organisation
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Sponsor type
University/education

ROR
https://ror.org/02j61yw88

Funder(s)

Funder type
University/education

Funder Name
Aristotle University of Thessaloniki

Alternative Name(s)
Aristotelian University, University of Thessaloniki

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Greece

Results and Publications

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

Intention to publish date
31/12/2021

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
Data sharing statement to be made available at a later date