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PLANES - placental growth factor led management of the small for gestational age fetus: a feasibility study

Submission date
15/01/2019

Recruitment status
No longer recruiting

Registration date
04/07/2019

Overall study status
Completed

Last Edited
12/08/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Being small for gestational age (SGA) in the womb is a common condition affecting 1 in 10 of all pregnant women. If not managed with careful monitoring it has been shown to be related to stillbirth (2 per 1000 women >37 weeks). At present there is no treatment available for these small babies and current management on the NHS consists of careful monitoring with ultrasound and heart rate tracings (CTG) and early delivery, usually offered around 37 weeks. Early delivery requires interventions such as 'starting off' (inducing) labour when most of these babies are still healthy. When a small baby is delivered early, even from 36 weeks onwards, it can increase the risk of them having later health and developmental difficulties. Delaying delivery by even a few weeks could be of benefit to a baby's development. It is possible that with further proof of the baby's health, such as how the placenta (afterbirth) is working, a small baby could be safely kept inside the womb for longer. Research studies using a blood test, sFlt-1/PlGF ratio, have shown that women with a normal test result are very unlikely to end up with a stillbirth. The sFlt-1/PIGF ratio provides information on how the placenta is functioning during pregnancy. If this test could be used for an SGA-affected pregnancy to reassure that the placenta is working well, a small baby could be safely left in the womb for longer, prolonging the pregnancy and improving the health of the baby. This would also allow the pregnancy to be managed in a more normal manner and may prevent the need to induce labour. This study aims to assess the feasibility and acceptability to women and clinical teams of using the sFlt-1/PIGF ratio for the management of SGA pregnancies. It is hoped that in the future this test could be used to identify which SGA babies are small but healthy and which are small and need early delivery.

Who can participate?
Women aged 16 and over with a single SGA pregnancy between 32+0 and 37+6 weeks of gestation

What does the study involve?
Participants provide a blood sample for sFlt-1/PIGF ratio testing. They are randomly allocated to either have their test results revealed to doctors or concealed (standard care only). This is in order to see how good the sFlt-1/PIGF ratio test is compared to standard NHS care. Participants

with an SGA baby and a normal sFlt-1/PlGF ratio have a repeat ultrasound and blood test every 2 weeks with a planned delivery delayed until 40 weeks. Participants with an SGA baby and an abnormal sFlt-1/PlGF ratio are offered delivery from 37 weeks, or sooner if necessary. Women allocated to standard care have their sFlt-1/PlGF ratio test result concealed from the clinical team with their pregnancy being managed as per the local NHS hospital policy.

What are the possible benefits and risks of participating?
The study has the potential benefit of reducing the likelihood of intervention in women carrying an SGA baby with a normal sFlt-1/PlGF ratio. This may allow normalisation of labour, less medicalisation of care, and greater control and choice for women as to the time of delivery than is currently offered. In addition in those women with an abnormal sFlt-1/PlGF ratio there will be greater recognition of clinical concern and more detailed ultrasound assessment will be performed which may improve the outcomes for the most high-risk pregnancies. Reducing the number of pre-term and early term deliveries is also expected to result in a reduced need for costly short and long-term care required by preterm and SGA infants. The potential risk of participation would be an adverse pregnancy outcome in women with an SGA baby and a normal sFlt-1/PlGF ratio. In the study women will be delivered later than would currently be offered under NHS care. To mitigate any potential risks women will be offered repeat ultrasound and sFlt-1/PlGF assessment every 2 weeks. If there are new concerns on ultrasound or the sFlt-1 /PIGF ratio becomes abnormal then care will be adjusted.

Where is the study run from?
1. Liverpool Women's Hospital (lead centre) (UK)
2. St Mary's Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2019 to July 2024

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

Who is the main contact?
Mr Gary Johnstone
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
255682

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 40734, IRAS 255682

Study information

Scientific Title
PLANES - placental growth factor led management of the small for gestational age fetus: a feasibility study

Acronym
PLANES

Study objectives
This is not a hypothesis driven study. The overall study objectives are:
1. To assess the feasibility of delivering sFlt-1/PIGF ratio led management of women with an SGA fetus
2. To assess the acceptability of such an approach to women and clinicians
3. To explore the feasibility/acceptability of the study design as an external pilot to inform the design of a subsequent randomised controlled trial (RCT)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/02/2019, North West – Liverpool East Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8235; nrescommittee.northwest-liverpooleast@nhs.net), ref: 18/NW/0857

Study design
Randomised; Interventional; Design type: Process of Care, Management of Care

Primary study design
Interventional

Study type(s)

Diagnostic

Health condition(s) or problem(s) studied
Small for gestational age fetus

Interventions
Participants will be recruited directly from the fetal medicine or maternity assessment units at the nominated research sites. All women who meet the eligibility criteria for this study will be invited to participate by their attending clinician and/or midwife. Once written informed consent has been provided participants will be registered onto the study and randomised by the research midwife/clinician at site.

Following randomisation women will be asked to provide a blood sample (20 ml) for assessment of sFlt-1/PlGF ratio, the result of which will be revealed (biomarker led) or concealed (standard care) from the attending clinician. A sFlt-1/PlGF ratio measurement will be carried out within the local NHS laboratory as per local procedure, with the result being available to the attending clinical team within 24 hours.

Within the revealed/biomarker led care group participants with a normal sFlt-1/PlGF ratio (<38pg /ml) will be advised that their risk of an adverse pregnancy outcome is low and will be offered delivery at 39+0 wGA. Women will be offered further ultrasound and sFlt-1/PlGF ratios every two2 weeks, to ensure that they do not become high risk, with the care pathway adjusted if necessary. Participants with an abnormal sFlt-1/PlGF ratio (>38pg/ml) will be advised to attend for detailed ultrasound assessment by a fetal medicine expert within 72 hours of the abnormal result being known. This assessment will involve fetal biometry and Dopplers of the Umbilical Artery (UA), Middle Cerebral Artery (MCA) and Ductus Venosus (DV). If Dopplers are normal then delivery will be advised from 37+0 weeks. If there is evidence of critical fetal compromise (absent end diastolic flow in the UA or absent a-wave in the DV) then delivery will be performed as soon as feasible. If fetal Dopplers are borderline (brain sparing or increased resistance in UA or DV), the Doppler will be repeated every 72hrs and delivery will be offered between 36+0 and 37+0 weeks.

Women assigned to the concealed/standard care pathway will have a sFlt-1/PlGF ratio taken but the result will be concealed from the clinical team with their pregnancy being managed as per the local NHS guideline with delivery from 37+0 weeks.

Once recruited, all participants will remain in the study until discharge from hospital or their due date whichever is sooner. The trialists will collect routine clinical data from all participants' notes and electronic hospital records for maternal and neonatal outcomes. Women who prefer not to be randomised will be offered the opportunity to give blood for a sFlt-1/PlGF ratio test with the result being concealed and not used to guide clinical management. Results from this pilot study along with health economic and qualitative elements will inform the design of a future large randomised controlled trial powered for adverse pregnancy outcome.

Intervention Type
Other

Primary outcome(s)
The feasibility of using a maternal biomarker (sFlt-1/PIGF ratio) to refine the care pathway for the management of pregnancies affected by SGA including:
1. Recruitment rate recorded as the number of eligible women who consent to participate in the

study during the 12 month recruitment period
2. Attrition rate assessed using the number of women who consent to participate and remain in the study until hospital discharge or their due date, whichever is sooner
3. Acceptability of biomarker led management to women and clinicians assessed by interviews /questionnaires (PLANES Women and Partner Questionnaire) with women and their birth partners following the consent process and clinician focus groups at the end of the 12-month recruitment period

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
31/07/2024

Eligibility

Key inclusion criteria
1. Women with a SGA fetus between 32+0 and 37+6 weeks of gestation
2. Singleton pregnancy
3. Age ≥16 years
4. 32+0 – 37+6 weeks of gestation
5. EFW <10th centile on ultrasound within preceding 72 hours

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
1. Unable to give informed consent
2. Known or suspected structural/chromosomal fetal abnormality
3. Absent or reversed EDF in Umbilical Artery on Doppler study

Date of first enrolment
14/03/2022

Date of final enrolment
31/01/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Liverpool Women's Hospital (lead centre)
Liverpool Women's NHS Foundation Trust
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
St Mary's Hospital
Manchester University NHS Foundation Trust
Oxford Road
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: PB-PG-0817-20021

Results and Publications

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date. To be determined with guidance from the funder, sponsor and the study steering committees.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		19/11/2020	12/08/2025	Yes	No
HRA research summary			28/06/2023	No	No