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EACH study: Evaluation of Array Comparative genomic Hibridisation in prenatal diagnosis of foetal anomalies

Submission date	Recruitment status	[_] Prospectively registered
24/06/2013	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/06/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
20/10/2017	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11729

Study information

Scientific Title
EACH study: Evaluation of Array Comparative genomic Hibridisation in prenatal diagnosis of foetal anomalies

Acronym
EACH

Study objectives
All pregnant women are offered ultrasound scans to detect fetal abnormalities, many of which are due to chromosome imbalances. Babies with chromosomal abnormalities have complex problems, usually resulting in developmental disability. Parents faced with this knowledge have to make difficult choices. Testing for chromosome problems involves an 'invasive' procedure (e. g. amniocentesis) which can cause miscarriage. Major chromosomal abnormalities can be detected quickly by a technique called PCR. Less common imbalances require the baby's cells to be grown (karyotyping) which is slow, labour intensive and only detects large (microscopic) imbalances. Array comparative genomic hybridisation (CGH) is a new molecular test that can rapidly detect smaller (sub-microscopic) imbalances. In children with developmental disability, array CGH has detected imbalances in 10% of cases. Limited experience of array CGH on fetal samples suggests it may detect 5-10% more chromosome imbalances than karyotyping. However performing and interpreting arrays is complex. The size of imbalances that can be detected depends on array design and not all imbalances cause problems some are inherited from a parent. Understanding the significance of a newly detected imbalance requires further tests on fetal and parental DNA. This study will recruit 1500 fetuses undergoing karyotyping because of a scan abnormality. Arrays will be performed and interpreted in 7 Genetics laboratories according to agreed guidelines. Clinicians/parents will be informed of large imbalances detected by array CGH but only where the outcome of such imbalance is known (based on the medical literature). In addition to determining if array CGH detects harmful chromosomal imbalances more often, more quickly and at less cost than karyotyping, the study will find out what parents and health professionals think of the new technology.

Ethics approval required
Old ethics approval format

Ethics approval(s)
04/01/2012, ref: 11/NE/0331

Study design
Non-randomised; Interventional; Design type: Diagnosis, Process of Care

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Diagnostic

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
Topic: Genetics Research and Congenital Disorders, Reproductive Health and Childb; Subtopic: Genetics Research and Congenital Disorders (all subtopics), Reproductive Health and Childb (all Subtopics); Disease: Genetics Research and Congenital Disorders, Reproductive Health & Childbirth

Interventions
Diagnosis & management of care, comparision of karyotyping test with Array CGH; Study Entry: Registration only

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Detection of pathogenic Copy number variants (CNVs); Timepoint(s): detection of pathogenic CNVs and chromosomal imbalances by array CGH and/or karyotyping

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/05/2012

Completion date
01/09/2014

Eligibility

Key inclusion criteria
1. Fetuses (singleton or dichorionic twin) undergoing conventional karyotyping by amniocentesis or Chorionic villus sampling (CVS) for clinical indications with:
1.1. one or more structural anomalies identified on an ultrasound scan* or
1.2. an isolated nuchal translucency (NT) =3.5 mm identified at the 11+2 to 14+1 wk ultrasound screening scan.
* Includes fetal growth restriction (defined as abdominal circumference >2 standard deviations below the mean for gestational age)
2. Only those fetuses with a normal qfPCR result, fetuses with a sex chromosome aneuploidy that is unlikely to explain the ultrasound anomaly e.g. XXX, XXY and XYY will undergo array CGH. This group has the highest risk of unbalanced chromosomal rearrangements [25] and recent array CGH studies suggest that they have the highest risk of pathogenic CNVs.

Cases will be recruited from selected Fetal Medicine Units (FMUs) in England and Wales.
Target Gender: Male & Female; Upper Age Limit 65 years ; Lower Age Limit 16 years

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 3000; UK Sample Size: 3000; Description: 1500 Maternal Consents 1500 Paternal Consents

Key exclusion criteria
1. Single or multiple ultrasound variants (or markers). In this context fetal cerebral ventriculomegaly (atrium = 10 mm) is classed as a structural anomaly not a normal variant.
2. Structural anomaly identified outside the time frame specified in the inclusion criteria
3. Participant declines to take part in the study
4. Participant is under the age of 16 years
5. Participant is unable to read English and understand the study information leaflet
6. Those fetuses with Triploidy, the common aneuploidies (Trisomy 13, 18, 21), or Monosomy X will be excluded from the study

Date of first enrolment
01/05/2012

Date of final enrolment
01/09/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Institute of Cellular Medicine
Newcastle Upon Tyne
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Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

Sponsor details
Northern Centre for Cancer Care
Freeman Road
High Heaton
Newcastle upon Tyne
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NE7 7DN

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Coordinating Centre; Grant Codes: 10/06/03

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2017		Yes	No