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Born early, breathe easy

Submission date 08/01/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 12/02/2016	**Overall study status** Completed	
Last Edited 06/03/2024	**Condition category** Neonatal Diseases	

Plain English summary of protocol

Background and study aims
This project looks at whether some babies born early can have long-term breathing problems as they go through childhood which have not yet been detected. Research on very premature babies has shown that their lungs may not work as well as babies born at, or earlier to, their due date. Work already done by the researchers of this project has also shown that some moderately premature babies are at risk of having breathing problems as they grow up. The next step of this research is to invite some families to participate in a study to look at possible reasons why children born early may have breathing problems. The researchers want to know whether there are differences in the structure and function of the airways in the children born prematurely compared to those born on time. If prematurely born children are different, they may benefit from closer follow-up and possibly some treatment to improve their breathing.

Who can participate?
Children (and families) aged between 7-12 who were born prematurely (at 34 weeks gestation or less)

What does the study involve
First of all, each child does some breathing tests (at home, if possible) and both them and their parents are asked to fill in some questionnaires about their daily life. A sample of saliva (spit) is also collected. The aim of the visit is to assess how many children have lower than expected results on the breathing test. Children will a lower than expected result are asked to take part in the next stage. For this stage, each child and their parents visit the laboratory on two occasions to have more detailed breathing tests before and after exercising on a stationary bicycle. After the first visit, each child is given an inhaler to use twice a day for 12 weeks. The type of inhaler they are given is allocated randomly and could be one containing fluticasone proprionate, a fluticasone proprionate/salmeterol xinafoate combination or a placebo (dummy inhaler). Any response to the inhaler treatment will be seen at the second visit. Finally, some children are invited to have a MRI scan of their lungs to look at how well they are working.

What are the benefits and risks?
The researchers aim to show that children born early have limitations in their lung function which may cause breathing problems. If so, they will be able to find out if treating with medicine is successful in easing the symptoms. Children born preterm have generally been ignored, however the evidence from this study may indicate to healthcare policy makers that closer

follow-up is required in these children; secondly, it may indicate that treatment should be considered an option in all children born preterm, (extremely or moderately) with reduced lung function. In the future, this surveillance and treatment may reduce the burden on NHS resources in terms of GP and hospital visits. As with all medicines, there are some small risks of side effects. However these are rare and often mild.

Where is the study run from?
Children's Hospital for Wales (UK)

When is study starting and how long is it expected to run for?
March 2015 to December 2019

Who is the main contact
Mr John Lowe

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-003712-20

Protocol serial number
2015-003712-20

Study information

Scientific Title
Respiratory Health Outcomes in Neonates - A randomised, double blind, double-dummy placebo-controlled trial of inhaled treatment to establish the mechanisms of prematurity-associated airway obstruction and inflammation

Acronym
RHINO

Study objectives
The overall aim is to establish the underlying mechanisms of chronic airway obstruction observed in symptomatic children who are born preterm and to establish if there are different phenotypes of this condition that do or do not respond to standard inhaled therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West - Central Bristol Research Ethics Committee, 26/11/2015, ref: 15/SW/0289

Study design
Single-centre, randomised, double blind, placebo controlled trial

Primary study design
Interventional

Study type(s)

Other

Health condition(s) or problem(s) studied
Prematurity-associated respiratory disease

Interventions
Random assignment to using one of the three following metered-dose inhalers
1. Fluticasone proprionate
2. Fluticasone proprionate/salmeterol xinafoate combination
3. Placebo

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
1. Fluticasone proprionate 2. Salmeterol xinafoate

Primary outcome(s)
The primary outcome will be the difference in pre and post treatment percent predicted FEV1 after 12 weeks of therapy between the active and placebo groups

Key secondary outcome(s))
1. Differences in measures of obstructive airway disease (pulmonary function tests)
2. Differences in response to exercise challenge between treatment groups.
3. Differences in biomarkers of airway inflammation between treatment groups
4. Differences in respiratory and neurological symptoms (questionnaire)
5. MRI parameters: apparent diffusion coefficient (ADC) between 3 comparison groups (preterm, FEV1 ≤85% at baseline; preterm control, FEV1 ±1 standard deviation from normal; and term control, FEV1 ±1 standard deviation from normal).
6. Pre- and- post treatment differences in objectively measured physical activity
7. Adverse events

All outcomes to be measured after 12 weeks of therapy between the active and placebo groups

Completion date
30/06/2020

Eligibility

Key inclusion criteria
1. Children aged 7-12 at the time of screening
2. Born at a gestational age ≤34 weeks (NB. Approximately n=50 term controls will also be invited)
3. Resident in the south Wales area whom, in the opinion of the Investigator, are possible to follow up
4. Fully informed proxy consent from parents/guardians and assent from child where possible

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
7 years

Upper age limit
12 years

Sex
All

Total final enrolment
53

Key exclusion criteria
1. Respiratory tract infection within the last three 3 weeks (will be asked to consider participating at a later date)
2. Congenital abnormalities
3. In the opinion of the Investigator have:
3.1. Severe cardiopulmonary defects, or
3.2. Neuromuscular disease, or
3.3. Severe neurodevelopmental impairment
Which prohibit the possibility of compliance with the study protocol

Date of first enrolment
01/05/2016

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Children's Hospital of Wales
Heath Park

Cardiff
United Kingdom
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Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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

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?
Results article		13/12/2021	10/01/2022	Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version 10	16/10/2018	22/08/2022	No	No
Statistical Analysis Plan	Trial Protocol and Statistical Analysis Plan		06/03/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes