

Born early, breathe easy

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| Submission date 08/01/2016 | Recruitment status No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol |
| Registration date 12/02/2016 | Overall study status Completed | <input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 06/03/2024 | Condition category Neonatal Diseases | <input type="checkbox"/> Individual participant data |

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 with 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 propionate, a fluticasone propionate/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

Contact name
Mr John Lowe

Contact details
Department of Child Health
School of Medicine
Cardiff University
Heath Park
Cardiff
United Kingdom
CF144XN

Type(s)
Scientific

Contact name
Prof Sailesh Kotecha

Contact details
Department of Child Health
School of Medicine
Cardiff University
Heath Park
Cardiff
United Kingdom
CF1 44XN

Type(s)
Public

Contact name

Ms Alison Jenkins

Contact details

North Wales Organisation for Randomised Trials in Health & Social Care)
Meirion Building
Normal Site
Bangor University
Gwynedd
Bangor
United Kingdom
LL57 2PZ
+44 (0)1248 382442
RHINO@bangor.ac.uk

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 propionate
2. Fluticasone propionate/salmeterol xinafoate combination
3. Placebo

Intervention Type

Drug

Phase

Phase IV

Drug/device/biological/vaccine name(s)

1. Fluticasone propionate
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 $\leq 85\%$ 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 impairmentWhich 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
CF144XN

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, 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

Date

Date

Peer

Patient-

| Output type | Details | created | added | reviewed? | facing? |
|---|--|------------|------------|-----------|---------|
| Results article | | 13/12/2021 | 10/01/2022 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |
| 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 |