ISRCTN17083028 https://doi.org/10.1186/ISRCTN17083028

RESPONSE: Recombinant surfactant protein D to prevent neonatal chronic lung disease – safety trial

Submission date
05/04/2023

Recruitment status
No longer recruiting

Registration date
26/07/2023

Overall study status
Completed

Last Edited
07/07/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Bronchopulmonary Dysplasia (BPD), also known as chronic lung disease (CLD), is a serious long-term lung condition that can affect up to 70% of infants born prematurely before 28 weeks of pregnancy. This is because their lungs have not fully developed, and they do not produce a soapy substance called surfactant. It is not clear why they develop CLD, but inflammation and infection have a role. Current surfactant replacement therapy consists of phospholipids and surfactant proteins B and C, but no surfactant protein A or surfactant protein D (SP-D). SP-D has anti-inflammatory and anti-infection properties, both of which play a role in the development of CLD. The RESPONSE study is a first-in-human study of recombinant SP-D (rfhSP-D), which is a manufactured version of SP-D that is a part of the naturally occurring protein. The study aims to find out the safest dose of rfhSP-D for premature infants (under 30 weeks gestation) who are at high risk of CLD, and how it helps to prevent CLD.

Who can participate?
Inborn infants born between 23 weeks and 0 days and 29 weeks and 6 days gestation requiring intubation or planned to be intubated for respiratory distress

What does the study involve?
Up to 24 participants will be recruited for the study. Each infant will receive up to three administrations of rfhSP-D, either 1 mg/kg, 2 mg/kg or 4 mg/kg. The infants will be enrolled in groups with a dose level increase in each group after it has been deemed safe to increase the dose level by an independent Data and Safety Monitoring Board and Study Steering Committee. Participants will continue to be monitored in the Neonatal Unit until discharge.

What are the possible benefits and risks of participating?
As this is the first study of rfhSP-D in humans, possible adverse reactions to this Investigational Medicinal Product are not known. The safety of the participants in this study is paramount. The lowest possible dose of the drug will be used in the first cohort and the dose will only be escalated after review of safety data by an independent Data and Safety Monitoring Board. Safety data will be regularly monitored throughout the study, and an individual baby will stop

receiving rfhSP-D if there are safety concerns. The study will be stopped if safety concerns meet pre-defined criteria.

The gastric and tracheal aspirates are routinely taken and usually, the sample is discarded, but we will use this sample for analysis.

The blood samples that are done, where possible, will be taken from any central lines that the baby has and otherwise, a heel lance will be done. These will be timed with routine care and blood tests to minimise discomfort for the baby. Standard comforting measures used when doing blood samples will be used.

Up to 4ml of blood will be collected in total in this study, in addition to routine blood tests that are done as part of clinical management. The volume of blood taken is considered to be low risk to participants as the samples are taken over time [depending on gestational age at enrolment] and alongside any routine clinical blood samples taken.

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
April 2023 to December 2025

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
The RESPONSE Clinical Trial Manager, cctu.response@ucl.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Prof Howard Clark

Contact details
University College London
Medical School Building
74 Huntley Street
London
United Kingdom
WC1E 6AU
+44 (0)207 679 0834
h.clark@ucl.ac.uk

Type(s)
Scientific

Contact name
Prof Howard Clark

Contact details
University College London
Medical School Building
74 Huntley Street
London
United Kingdom
WC1E 6AU
+44 (0)207 679 0834
h.clark@ucl.ac.uk

Type(s)
Public

Contact name
Dr RESPONSE Clinical Trial Manager

Contact details
-
London
United Kingdom
-
None available
cctu.response@ucl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2021-001824-16

Integrated Research Application System (IRAS)
1004422

ClinicalTrials.gov (NCT)
NCT05898633

Protocol serial number
18/0564, IRAS 1004422

Study information

Scientific Title
RESPONSE - Phase I safety trial of recombinant surfactant protein D to prevent neonatal chronic lung disease

Acronym
RESPONSE

Study objectives
Current study hypothesis as of 07/08/2024:

The main objectives of the RESPONSE trial are to:
1. To assess the safety profile of rfhSP-D across 3 dose levels based on the occurrence of dose-limiting events (DLEs)
2. To establish the Recommended Phase II Dose (RP2D) of rfhSP-D for preterm infants born at a gestational age of <30 weeks

The trial will also aim:
1. To assess the safety profile of rfhSP-D across 3 dose levels based on the occurrence of SAE /AEs
2. To evaluate systemic absorption of rfhSP-D using serial measurements of rfhSP-D in serum and its continued presence in tracheal fluid
3. To determine the effect of rfhSP-D on inflammatory markers in the lung secretions (eg. cell counts of neutrophils, macrophages, MMPs, neutrophil elastase, IL-8, IL-6, IL-1)
4. To compare the clinical effects of endotracheal administration of rfhSP-D on physiological and intensive care parameters in treated infants in this trial with non-treated infants from a parallel observational study of untreated infants.

_____

Previous study hypothesis:

The main objectives of the RESPONSE trial are to:
1. To assess the safety profile of rfhSP-D across 3 dose levels based on the occurrence of dose-limiting events (DLEs)
2. To establish the Recommended Phase II Dose (RP2D) of rfhSP-D for preterm infants born at a gestational age of <28 weeks

The trial will also aim:
1. To assess the safety profile of rfhSP-D across 3 dose levels based on the occurrence of SAE /AEs
2. To evaluate systemic absorption of rfhSP-D using serial measurements of rfhSP-D in serum and its continued presence in tracheal fluid
3. To determine the effect of rfhSP-D on inflammatory markers in the lung secretions (eg. cell counts of neutrophils, macrophages, MMPs, neutrophil elastase, IL-8, IL-6, IL-1)
4. To compare the clinical effects of endotracheal administration of rfhSP-D on physiological and intensive care parameters in treated infants in this trial with non-treated infants from a parallel observational study of untreated infants.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/06/2023, London - Brent Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London , E20 1JQ, United Kingdom; +44 (0)20 7104 8128, (0)207 104 8131 ; brent.rec@hra.nhs.uk), ref: 23/LO/0381

Study design
Phase I dose-ranging safety study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bronchopulmonary dysplasia; congenital, hereditary, and neonatal diseases and abnormalities

Interventions
Recombinant fragment of human surfactant protein D (rfhSP-D) administration. This is a single-arm trial with the administration of rfhSP-D. All participants will be administered IMP via an endotracheal tube in 1-3 doses in the first 24-48hrs after birth whilst the infant is still intubated and ventilated.
A dose escalation design from 1mg/kg to 4mg/kg will be used. Infants are enrolled in cohorts of three, with the first cohort receiving the lowest dose of 1mg/kg.
Participants are followed up until they are discharged from the hospital.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
Recombinant surfactant protein D (rfhSP-D)

Primary outcome(s)
Current primary outcome measure as of 07/08/2024:

The following primary outcome measures will be measured using the occurrence of dose-limiting events (DLEs) recorded in the patient study records until 3 days post-last administration of the investigational medicinal product (IMP):
1. Safety profile of recombinant surfactant protein D (rfhSP-D) across 3 dose levels
2. Recommended phase II dose (RP2D) of rfhSP-D for preterm infants born at a gestational age of <30 weeks

———

Previous primary outcome measure:

The following primary outcome measures will be measured using the occurrence of dose-limiting events (DLEs) recorded in the patient study records until 3 days post-last administration of the investigational medicinal product (IMP):
1. Safety profile of recombinant surfactant protein D (rfhSP-D) across 3 dose levels
2. Recommended phase II dose (RP2D) of rfhSP-D for preterm infants born at a gestational age of <28 weeks

Key secondary outcome(s))
The following secondary outcome measures will be measured using patient study records for a follow-up of 40 weeks post-menstrual age, or hospital discharge, whichever is soonest:
1. Safety profile of rfhSP-D across 3 dose levels based on the occurrence of SAE/AEs
2. Systemic absorption of rfhSP-D using serial measurements of rfhSP-D in serum and its

continued presence in tracheal fluid
3. Effect of rfhSP-D on inflammatory markers in the lung secretions (eg. cell counts of neutrophils, macrophages, MMPs, neutrophil elastase, IL-8, IL-6, IL-1)
4. Clinical effects of endotracheal administration of rfhSP-D on physiological and intensive care parameters in treated infants in this trial with non-treated infants from a parallel observational study of untreated infants

Completion date
31/12/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/08/2024:

1. Inborn infants born between 23 weeks and 0 days and 29 weeks and 6 days gestation
2. Infant must be intubated or planned to be intubated for respiratory distress at the time of eligibility check, and this should be done within 12 hours from the time of birth
3. Receiving standard surfactant therapy
4. Clinically stable on mechanical ventilation. Stability is defined at the time of IMP instillation and is defined below
5. Written informed consent from parents/guardians/person with legal responsibility

Definition of stability:
1. Blood gases within the normal range for preterm infants (pH>7.20; paCO2 <60mmHg)
2. Mean blood pressure with or without inotropic support at least gestational age or above (mmHg)
3. No evidence of a pneumothorax
4. Clinical observations within acceptable range for an infant of that gestational age
5. No stability concerns from the attending neonatologist

———

Previous inclusion criteria:

1. Inborn infants born between 23 weeks and 0 days and 27 weeks and 7 days gestation
2. Infant must be intubated or planned to be intubated for respiratory distress at the time of eligibility check, and this should be done within 12 hours from the time of birth
3. Receiving standard surfactant therapy
4. Clinically stable on mechanical ventilation. Stability is defined at the time of IMP instillation and is defined below
5. Written informed consent from parents/guardians/person with legal responsibility

Definition of stability:
1. Blood gases within the normal range for preterm infants (pH>7.20; paCO2 <60mmHg)
2. Mean blood pressure with or without inotropic support at least gestational age or above (mmHg)
3. No evidence of a pneumothorax
4. Clinical observations within acceptable range for an infant of that gestational age
5. No stability concerns from the attending neonatologist

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
18

Key exclusion criteria
1. Congenital anomalies i.e any major antenatal diagnosed congenital abnormalities such as congenital heart disease, suspected or known chromosomal abnormalities
2. Parents/legal guardians unable to give consent due to learning or other difficulties
3. Infants requiring only CPAP support without the need for surfactant replacement therapy, i.e. without endotracheal intubation
4. Infants born in very poor conditions and judged too sick or unstable to be included (high risk of mortality) in an experimental first-in-human study, for example, infants that are requiring maximal intensive care therapy and have findings such as a grade IV intraventricular haemorrhage that is likely to be life-limiting
5. Infants that are born out of the participating site
6. Participation in any other interventional study (participation in an observational study is permissible)

Date of first enrolment
06/04/2024

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research council

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 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