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A randomised, double-blind, parallel group, placebo controlled, trial of Bactek for the prevention of lower respiratory tract infections in preterm infants

Submission date
24/05/2024

Recruitment status
Recruiting

Registration date
01/08/2024

Overall study status
Ongoing

Last Edited
04/02/2026

Condition category
Respiratory

[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
Babies born early or prematurely have under-developed lungs. Many need help with their breathing after birth and some go on to have lifelong lung problems. Premature babies will get infections after discharge, which they generally deal with well. The problem is that over half get chest infections which further damage the lungs. There are very few treatments available to prevent viral chest infections except against the virus called RSV (Respiratory Syncytial Virus). We want to use a new approach to prepare the babies' immune system to fight chest infections. Bactek (MV-130) is an oral spray containing harmless dead bacteria, so it works like a vaccine. The dead bacteria should help the baby build a strong immune system, preventing further damage to the lungs by helping fight chest infections. Studies show Bactek decreases chest infections and wheezing safely in children and babies. Only some premature babies have been studied so far, so a larger study is needed to show if Bactek works in premature babies born at less than 30 weeks' of gestation.

We want to collect data to show if Bactek spray decreases the number of visits to the GP, A&E or hospital admissions for chest infections in premature babies when compared to babies who get a placebo (dummy) spray. We will do a study called a blinded, randomised, placebo-controlled trial.

We wish to include 542 babies to show if chest infections decrease from 55% (the current rate) to 40%. If this treatment works, there will be large savings and it will benefit the parents and babies.

Who can participate?
Babies born at a gestational age ≤29+6 weeks (including infants born as one of a multiple births)

What does the study involve?
After consent from parents, we will allocate babies to one of two treatments. One group will get

Bactek and the other a placebo (treatment spray that looks the same but does not contain dead bacteria). Parents and researchers will not know which group the baby is in. The treatment will be given daily from when the baby reaches 37 weeks' corrected gestation (close to their "due date") until they are one year from their expected due date.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
The research team will be available at all times during the study to watch closely for possible health problems that may occur and to answer any questions. Parents are advised to inform study staff about any side effects or health problems whilst taking part in the study, and advised to report them, even if they do not think that the side effects are caused by the study medicine.
Nose swab: may cause some discomfort but should not be painful.
Blood sampling: small amounts of blood will be taken, and where possible, blood sampling will be aligned to a clinically required blood test. They will be advised there may be a little discomfort, bruising, bleeding or swelling where the needle enters the skin. Staff are trained in this procedure and will attempt to minimise discomfort or distress that may be experienced to perform the procedure quickly and as painlessly as possible. Not all babies will have blood taken.
Lung function testing: This will be carried out whilst the babies are asleep and will not cause any distress,
Bactek (MV-130) side effects are explicitly detailed in the Summary of product characteristics. To ensure any early adverse reactions are identified, a safety run-in period will take place for the first 4 participants recruited. At least one week of dosing must be completed prior to initiating treatment in each subsequently randomised participant. All participants are under medical review for the duration of the trial.
All Participants are informed in advance about the risks during a detailed conversation and receive an emergency card with the relevant contact details of the site trial team.

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
March 2024 to March 2028

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

Who is the main contact?
Dr Sarah Kotecha, Trial Manager, kotechasj@cardiff.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007696

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
1939-23, IRAS 1007696, CPMS 55712

Study information

Scientific Title
A randomised, double-blind, parallel group, placebo controlled, trial of Bactek for the prevention of lower respiratory tract infections in preterm infants

Acronym
BALLOON

Study objectives
Current study hypothesis as of 07/03/2025:
Primary objective:
To investigate if sublingual Bactek spray, when compared to placebo, decreases the risk of

health professional diagnosed LRTIs (after unscheduled visits to general practitioners (GPs), accident and emergency departments (A&Es) and hospital admissions) between term-equivalent 37-43 weeks' gestation or discharge if earlier and one year of corrected age.

Secondary objective:
1. To establish if sublingual Bactek spray is superior to placebo in decreasing the number of health professional diagnosed LRTIs between term-equivalent 37 weeks' gestation or discharge if earlier and one year of corrected age.
2. To establish if sublingual Bactek spray is superior to placebo in increasing the time to first health professional diagnosed LRTI between term-equivalent 37 weeks' gestation or discharge if earlier and one year of corrected age.
3. To establish if sublingual Bactek spray is superior to placebo in preventing parent-reported, health professional confirmed, wheezing from 37-43 weeks' corrected gestation or discharge if earlier to one year of corrected age in infants born at ≤29+6 weeks' gestational age.
4. To compare the use of respiratory medications including inhalers (bronchodilators, inhaled corticosteroids), antibiotics and systemic corticosteroids between the two groups.
5. To investigate the effect of Bactek on growth (weight, length and head circumference) between the two groups.
6. To establish effects of LRTI on the family, including time missed from work and/or nursery time missed for the infants.
7. To explore differential intervention effects by gestational age and anti-RSV prophylaxis.
8. To assess safety (volume of serious adverse events).

Previous study hypothesis:
Primary objective:
To investigate if sublingual Bactek spray, when compared to placebo, decreases health professional diagnosed LRTIs (after unscheduled visits to general practitioners (GPs), accident and emergency departments (A&Es) and hospital admissions) between term-equivalent 37 weeks' gestation and 1 year of corrected age.

Secondary objective:
1. To establish if sublingual Bactek spray is superior to placebo in preventing parent-reported, health professional confirmed, wheezing from 37 weeks' corrected gestation to one year of corrected age in infants born at <30 weeks' gestational age.
2. To compare the use of respiratory medications including inhalers (bronchodilators, inhaled corticosteroids), antibiotics and systemic corticosteroids between the two groups.
3. To establish effects of LRTI on the family, including time missed from work and/or nursery time missed for the infants.
4. To explore differential intervention effects by gestational age, anti-RSV prophylaxis, and centre.
5. To assess safety (volume of serious adverse events).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 29/07/2024, Wales Research Ethics Committee 3 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2922 940963; wales.rec3@wales.nhs.uk), ref: 24/WA/0181

Study design

Interventional double-blind randomized controlled trial

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Respiratory outcomes after premature birth including lower respiratory tract infections and wheeze.

Interventions
The active IMP and the placebo are sublingual sprays. The placebo is identical to the active IMP except for the absence of the active ingredients.

Active IMP: A sublingual spray comprising of a polybacterial preparation of heat-inactivated Staphylococcus aureus, S. epidermidis, Streptococcus pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae and Moraxella catarrhalis (Bactek™, Inmunotek, Spain).

Placebo: A sublingual spray comprising of all excipients of the active IMP, aside from the inactivated bacteria.

Dosage: 300 FTU/mL (2x 150 FTU/mL sprays), once daily, from 37 weeks corrected age or discharge if earlier up to 1 year of corrected age

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Bactek™, Inmunotek, Spain

Primary outcome(s)
Current primary outcome measure as of 07/03/2025:
The presence/absence of parent-reported, health professional-confirmed unscheduled visits for LRTIs to GPs, A&Es and hospital admissions between 37-43 weeks' corrected age (or discharge if earlier) and one-year corrected age.

Previous primary outcome measure:
The number of parent-reported, health professional-confirmed unscheduled visits for LRTIs to GPs, A&Es, paediatric assessment units and hospital admissions between 37 weeks' corrected age (or discharge if earlier) and 1-year corrected age
"Corrected age" is calculated using the expected date of delivery, therefore taking the degree (number of weeks of prematurity) into account.

An LRTI will be defined as:
Fever (≥38°C) or a runny nose (rhinitis) for at least 12 hours, plus one additional symptom from the following:

moist cough
wheezing
shortness of breath
tachypnoea
intercostal recession
poor feeding

The LRTI will be considered to be a new episode if there is an intervening period of at least 72 hours between episodes when the infant is well.

Key secondary outcome(s))

Current secondary outcome measures as of 07/03/2025:
1. Number of parent-reported, health professional-confirmed unscheduled visits for LRTIs to GPs, A&Es and hospital admissions between 37 weeks' corrected age (or discharge if earlier) and one-year corrected age.
2. Time to first episode of parent-reported, health professional-confirmed unscheduled visits for LRTIs to GPs, A&Es and hospital admissions between 37-43 weeks' corrected age (or discharge if earlier) and one-year corrected age.
3. Parent-reported wheeze episode between 37-43 weeks' corrected age or discharge if earlier and one-year corrected age.

Wheeze episode is defined as an episode of wheezing:
1. that lasts at least one day with a sign of increased work of breathing such as shortness of breath, cough, or chest retraction or with any combination of these additional symptoms.
1.1 To establish the effect of Bactek on growth between the two groups
1.2 Parent-reported use of respiratory medications including bronchodilators, antibiotics and systemic corticosteroids
1.3 Parent(s)/guardian(s) reported time missed from work and/or nursery time missed for the infant
1.4 Volume of adverse reactions
1.5 Identification of virus(es) associated with LRTIs

Previous secondary outcome measures:
1. Parent-reported wheeze episode between 37 weeks' corrected age and 1-year corrected age. Wheeze episode is defined as an episode of wheezing that lasts at least one day with a sign of increased work of breathing such as shortness of breath, cough, or chest retraction or with any combination of these additional symptoms. A WheezeScan device will be provided to parent(s) /guardian(s) and may be used to help parents detect these symptoms.
2. Parent-reported use of respiratory medications including bronchodilators, antibiotics and systemic corticosteroids
3. Parent(s)/guardian(s) reported time missed from work and/or nursery time missed for the infant
4. Volume of adverse reactions
5. Identification of virus(es) associated with LRTIs
6. Growth (weight, length and head circumference)

Completion date

31/03/2028

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 07/03/2025:
1. Birth at gestational age ≤29+6 weeks'
2. Follow-up is likely to be feasible
3. Survival to one year corrected age is anticipated
4. In addition to infants without an eventful course, the following groups are eligible for inclusion:
5. Infants diagnosed with bronchopulmonary dysplasia
6. Infants discharged home on oxygen
7. Infants who have had necrotising enterocolitis
8. Infants on oral or nasogastric tube feeding
9. Infants with treated patent ductus arteriosus
10. Infants with neurological disorders
11. Infants with resolved sepsis

Previous participant inclusion criteria:
1. Birth at gestational age ≤29+6 weeks (including infants born as one of a multiple births)
2. In the opinion of the PI, follow-up is likely to be feasible (i.e routine outpatient appointments will be at the recruiting site, locality of baby's residence so follow up to one year corrected age is possible.)
3. Survival to 1 year corrected of age is anticipated

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
0

Key exclusion criteria
Current participant inclusion criteria as of 07/03/2025:
1. Presence of major surgical, cardiac or congenital abnormalities (not including patent ductus arteriosus or patent foramen ovale)
2. Contraindication of Bactek™ as specified in the Investigator's Brochure
3. Participation in other interventional trial that precludes participation in BALLOON
4. Primary immune deficiencies

Previous participant inclusion criteria:
1. Presence of major surgical, cardiac or congenital abnormalities (not including patent ductus arteriosus or patent foramen ovale)
2. Contraindication of Bactek™ as specified in the Investigator's Brochure
3. Participation in other interventional trial that precludes participation in BALLOON

Date of first enrolment
17/02/2025

Date of final enrolment
31/08/2026

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
Wales
CF14 4XW

Study participating centre
Royal Victoria Infirmary
Claremont Wing Eye Dept
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
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NE1 4LP

Study participating centre
Hull Royal Infirmary
Anlaby Road
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HU3 2JZ

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
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England
BS10 5NB

Study participating centre
Medway Maritime Hospital
Windmill Road
Gillingham
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ME7 5NY

Study participating centre
Queen Alexandra Hospital
Southwick Hill Road
Cosham
Portsmouth
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PO6 3LY

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
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PR2 9HT

Study participating centre
Arrowe Park Hospital
Arrowe Park Road
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CH49 5PE

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
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LE1 5WW

Study participating centre
Royal Sussex County Hospital
Eastern Road
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England
BN2 5BE

Study participating centre
St Richards Hospital
Spitalfield Lane
Chichester
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PO19 6SE

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
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Study participating centre
University Hospitals Birmingham NHS Foundation Trust
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BN11 2DH

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WF1 4DG

Study participating centre
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DA2 8DA

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available