

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

<b>Submission date</b> 24/05/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 01/08/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 18/06/2025	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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  $\leq 29+6$  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](mailto:kotechasj@cardiff.ac.uk)

## Contact information

**Type(s)**

Public, Scientific, Principal Investigator

**Contact name**

Prof Sailesh Kotecha

**Contact details**

UGT155, UHW, Heath Park  
Cardiff  
United Kingdom  
CF14 4XN  
-  
kotechas@cardiff.ac.uk

**Type(s)**

Public, Scientific

**Contact name**

Dr Sarah Kotecha

**Contact details**

Trial Manager  
Cardiff  
United Kingdom  
CF14 4XN  
-  
kotechasj@cardiff.ac.uk

## Additional identifiers

**EudraCT/CTIS number**

Nil known

**IRAS number**

1007696

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

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  $\leq 29+6$  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

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Community, Hospital

**Study type(s)**

Efficacy

**Participant information sheet**

**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

**Pharmaceutical study type(s)**

Not Applicable

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Bactek™, Inmunotek, Spain

**Primary outcome measure**

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 ( $\geq 38^{\circ}\text{C}$ ) 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.

## **Secondary outcome measures**

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)

**Overall study start date**

01/03/2024

**Completion date**

31/03/2028

## **Eligibility**

**Key inclusion criteria**

Current participant inclusion criteria as of 07/03/2025:

1. Birth at gestational age  $\leq 29+6$  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  $\leq 29+6$  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

**Age group**

Neonate

**Sex**

Both

**Target number of participants**

542

**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**

England

United Kingdom

Wales

**Study participating centre**

**University Hospital of Wales**

Heath Park

Cardiff

United Kingdom

CF14 4XW

**Study participating centre**

**Royal Victoria Infirmary**

Claremont Wing Eye Dept

Royal Victoria Infirmary

Queen Victoria Road

Newcastle upon Tyne

United Kingdom

NE1 4LP

**Study participating centre**

**Hull Royal Infirmary**

Anlaby Road



Hull  
United Kingdom  
HU3 2JZ

**Study participating centre**  
**Southmead Hospital**  
Southmead Road  
Westbury-on-trym  
Bristol  
United Kingdom  
BS10 5NB

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

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

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

**Study participating centre**  
**Arrowe Park Hospital**  
Arrowe Park Road  
Wirral  
United Kingdom  
CH49 5PE

**Study participating centre**  
**Leicester Royal Infirmary**  
Infirmary Square  
Leicester  
United Kingdom  
LE1 5WW

## Sponsor information

**Organisation**  
Cardiff University

**Sponsor details**  
30-36 Newport Road  
Cardiff  
Wales  
United Kingdom  
CF24 0DE  
-  
shawc3@cardiff.ac.uk

**Sponsor type**  
University/education

**Website**  
<http://www.cardiff.ac.uk/>

**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**

**Publication and dissemination plan**

Peer reviewed scientific journals

Conference presentation

Publication on website

Submission to regulatory authorities

**Intention to publish date**

31/03/2029

**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