Guidance Sheet 4:

Study intervention

Centre for Trials Research
Canolfan Ymchwil Treialon

BALLOON

Treatment spray and placebo spray

BALLOON is a placebo-controlled trial. 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.

The treatment spray is 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).

The matched placebo spray is a sublingual spray comprising of all excipients of the active IMP, aside from the inactivated bacteria.

Two-phase III trials in children with wheezing attacks and adults with COPD have shown Bactek administration to be safe.

a) Packaging

Bactek or placebo will be packaged as pairs of sprays, which in combination provide sufficient supply for at least 3 months of treatment. 5 boxed pairs of sprays will be presented in a “treatment pack”, sufficient to cover the treatment period plus one back up pair of sprays. IMP for each recruited infant shall be prescribed and dispensed on a 3-monthly basis.

b) Storage

The BALLOON medication is an Investigational Medicinal Product (IMP) and should always be stored appropriately.

Correct Storage at Site

In the BALLOON trial there is provision for IMP being held in pharmacy. At recruiting sites, a stock of IMP will be held in pharmacy. It is essential that storage requirements are observed in all cases:

1. IMP should be stored at 2 and ≤8°C and stored in a designated area for IMPs. Records will be maintained in accordance with that pharmacy's standard operating procedures.
2. Short temperature deviations during transport or storage are not critical and no further actions are required: In the case of temperature deviations >8°C, stability data has shown that the IMP is stable and safe for use for up to 24 months, even if stored up to 25°C for 3 months.

c) Pack Allocation

Each infant will be allocated a treatment pack ID number during randomisation (see Guidance Sheet 3 – Randomisation).

d) Treatment prescribing and dispensing

Once it has been confirmed that a baby meets the eligibility criteria, written informed consent has been obtained, and the baby has been randomised, the BALLOON trial medication can be prescribed. The IMP prescription will be submitted to the pharmacy, specifying the pack ID to be dispensed.

IMP for each recruited infant shall be prescribed and dispensed on a 3-monthly basis. Babies will be allocated a **five-digit** Treatment Pack ID number during randomisation. This number will correspond to a pack containing 2 sprays of either Bactek or placebo. You will not know whether the baby has been allocated Bactek or placebo. If necessary unblinding is possible (**see guidance sheet 8: Withdrawal & Unblinding**).

Packs of trial medication **must only be** administered to the baby to whom it was allocated.

The allocated medication will be:
BALLOON IMP: 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. NB They must be at least 34 weeks' corrected gestation to start the spray.

Please give 2 sprays under the tongue once a day at approximately the same time.
Please give the spray at least 30 minutes before and after any food or drinks.
Do not brush or rinse the mouth within 30 minutes of giving the spray.

How to give the spray

- Remove the plastic seal from the bottle.
- Gently shake the bottle.
- Rotate the nozzle sideways. Spray 3 or 4 times to ensure pump fills up (only when starting the bottle).
- Try to lift the tongue and direct the nozzle under the tongue and spray twice.
- Rotate the nozzle back to it's original vertical position.
- Return bottle to the box and return the spray to the fridge.
- When first bottle is finished please start using the second bottle.

e) Starting supplementation in hospital

The study supplement and study procedures must only be started once informed consent and randomisation have been completed. Infants should commence the spray if they are still inpatients on the NNU at 37 weeks' corrected gestation.

f) Starting supplementation at home and supplementation supply at discharge

At discharge, parents should be provided with a 3 months' supply of the spray. They must be at least 34 weeks' corrected gestation to start the spray. After discharge home further supplement will be supplied by the research nurse, either delivered directly to the family home or collected at hospital visits. The parents should be reminded to keep the used sprays for collection and weighing by the research nurses.

g) Concomitant medication

No drug interactions are expected due to the nature of Bactek and it's mechanism of absorption. There are no prohibited medications.