STep-wise Anti-inflammatory Reliever Therapy-Children's Asthma REsearch (START CARE) study

An open-label randomised controlled trial of Budesonide-formoterol maintenance and/or reliever therapy vs standard therapy of Budesonide maintenance or Budesonide-formoterol maintenance, both with Terbutaline reliever, in mild, moderate and severe childhood asthma

Rationale

One in seven children in NZ receive treatment for asthma, with over 3,500 children admitted to hospital with asthma exacerbations annually.

The traditional approach to managing asthma is to prescribe a maintenance ICS or ICS-LABA inhaler and/or a SABA reliever, taken as needed for symptom relief. Inhaled corticosteroid (ICS)-formoterol, used as both maintenance and/or reliever therapy, is now the GINA-preferred treatment option for adolescents and adults with asthma across all treatment steps. Combining an ICS with a fast-onset beta$_2$-agonist, such as formoterol, in a single inhaler offers a potential solution to protect against the dangers of beta$_2$-agonist monotherapy and poor ICS adherence, by ensuring that an ICS dose is delivered with each "reliever" inhalation. If comparable efficacy with ICS-formoterol maintenance and/or reliever therapy is shown in childhood asthma, then implementation of this regimen would markedly reduce the burden of asthma in all children.

Study design

The START CARE study is an investigator-initiated, multi-centre, New-Zealand based, open-label randomised control trial, designed by a team of international asthma experts and paediatricians. We plan to enrol 400 children aged five to 11 years with mild, moderate and severe asthma (corresponding to GINA step 2, 3 and 4) with ICS or ICS-LABA maintenance plus SABA reliever therapy. Participants will be enrolled for 56 weeks (including a 4-week run-in period to ensure adequate Turbuhaler technique) and randomised to receive either:

- Budesonide 100mcg DPI (Pulmicort Turbuhaler®, AstraZeneca) maintenance or Budesonide-formoterol 100/6mcg DPI (Symbicort Turbuhaler®, AstraZeneca) maintenance, each with Terbutaline 500mcg DPI (Bricanyl Turbuhaler®, AstraZeneca) reliever, one inhalation as needed. Drug and dose of maintenance therapy adjusted according to GINA step at study entry
- Budesonide-formoterol 100/6mcg DPI (Symbicort Turbuhaler®, AstraZeneca) maintenance AND/OR reliever use as needed. Regimen and dose will be adjusted according to GINA step at study entry

The primary outcome is the difference in the rates of asthma attacks between the two treatment arms. Participants will attend six in-person visits during the study (at 3-monthly intervals) at the [study site]. Visit procedures include Turbuhaler training and assessment of technique, asthma review (including asthma exacerbations, time off school/work), weight and height measurement, completing asthma questionnaires and performing lung function tests.

The START CARE study is sponsored by the MRINZ, and funded by AstraZeneca (ESR-22-21744), and the study team includes academic paediatricians from New Zealand, the UK and Australia. It is approved by the Northern B Health and Disability Ethics Committee (2022 FULL 13221) and the Standing Committee on Therapeutic Trials (2022 SCOTT 13289).

Benefits to participants

- Parent(s)/guardian(s) of participants will be reimbursed at least $50 per in-person visit attended. This is to cover the cost of travel-related expenses (fuel, parking etc). In addition to this reimbursement, parent(s)/guardian(s) will be paid a stipend/honorarium of $200 to recognise the time taken out of work/usual activities to attend each visit. The children will receive a badge at visit 1 and stickers and a $25 gift card or book voucher at each visit as a thank you for their help. They will also receive a certificate at Visit 6.
- Participants will receive regular asthma education, training, and contact from an experienced team of asthma researchers.
- Participants enrolled into research studies tend to have better outcomes.
- Medication is provided free of charge throughout the study.
- There is no obligation to take part and participants can withdraw at any time.

Benefits to Schools

- You will be assisting with world-leading research that could help to reduce the:
    - Asthma burden in children, including reducing time missed from school due to asthma
    - Asthma burden on school staff, due to time spent managing poorly controlled asthma