Pharmacogenetics Use For Further treatment Improvement in childreN

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Children with asthma carrying a risk variant might benefit more from doubling inhaled corticosteroids (ICS) thant from adding LABAs.

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21847

Bron
NTR

Verkorte titel
PUFFIN

Aandoening

Uncontrolled asthma, LABA response heterogeneity

Ongecontroleerd astma, LABA respons heterogeniteit

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC)
Overige ondersteuning: Longfonds

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Improvement of asthma control based on repeated measurement analysis of (childhood)-Asthma Control Test after 3 months

Toelichting onderzoek

Achtergrond van het onderzoek

Introduction

There is large heterogeneity in treatment response to asthma medication and a one-size fits all approach based on current guidelines might not fit all children with asthma. It is expected that children with one or more variant alleles (Arg16Arg and Arg16Gly) within the beta2 adrenergic receptor (ADRB2) gene coding for the beta2-receptor have a higher risk to poorly respond to long-acting beta2-agonists (LABA) comparing to the Gly16Gly wildtype.

Aims

To study whether ADRB2 genotype-guided treatment will lead to improvement in asthma control in children with uncontrolled asthma on inhaled corticosteroids compared with usual care.

Design

A multicentre, double-blind, precision medicine, randomized trial will be carried out within 15 Dutch hospitals. 310 asthmatic children (6-17 years of age) not well controlled on a low dose of inhaled corticosteroids (ICS) will be included and randomized over a genotype-guided and a non-genotype-guided(control) arm. In the genotype-guided arm children with Arg16Arg and Arg16Gly will be treated with double dosages of ICS and with the Gly16Gly wildtype with add on LABA. In the control arm children will be randomized over both treatment options. Lung function measurements, questionnaires focussing on asthma control (ACT/c-ACT) and quality of life, will be obtained in three visits within 6 months. The primary outcome will be improvement in asthma control based on repeated measurement analysis of c-ACT or ACT scores in the first three months of the trial. Additional cost effectiveness studies will be performed.

Conclusion

Currently, pharmacogenetics is not used in paediatric asthmas. This trial may pave the way to implement promising results for genotype-guided treatment in paediatric asthma in clinical practice.

Doel van het onderzoek

Children with asthma carrying a risk variant might benefit more from doubling inhaled corticosteroids (ICS) thant from adding LABAs.

Onderzoeksopzet

The study consists of 3 clinical visits (t=0, t=3 months, t=6 months) and monthly online questionnaires

Onderzoeksproduct en/of interventie

Participants will be randomized to 1) a genotype-guided treatment arm or 2) a usual care (non-genotype guided) control arm. In the genotype guided arm, children will be treated based on their genotype of ADRB2 (single nucleotide polymorphism rs1042713). Children homozygous for the risk variant (Arg16Arg) and heterozygotes (Arg16Gly) will be treated with doubling dosages of their ICS. Children homozygous for the wild type allele (Gly16Gly) will receive LABA as add-on to low dose ICS. In the control arm, children will be randomized between doubling ICS dosage or adding LABA, the two most common chosen options among respiratory paediatricians in the Netherlands when children are uncontrolled depsite low dosages of ICS.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Between 6-18 years of age

- Doctor's diagnosis of asthma based on FEV1 reversibility >= 12% ever and/or bronchial hyperresponsiveness ever

- Current asthma symptoms (based on ACT (>= 12 years) or C-ACT (< 12 years) score <= 19

- ICS use >= 3 months before inclusion (start dosage ICS, treatment step 2 according to childhood asthma guideline NVK)

- Adequate inhalation technique

- Self-assessed good adherence to maintenance asthma treatment

- Understanding of the Dutch language

- Internet access at home, willing to fill in internet questionnaires

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Active smoking

- Congenital heart disease

- Serious lung disease other than asthma (Cystic Fibrosis, Primairy Ciliary Dyskinesia, congenital lung disorders, severe immune disorders, severe trancheamalacia)

- LABA use in past 6 months

- Omalizumab use

- ICU admission in the previous year

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2018
Aantal proefpersonen:	310
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6539
NTR-old	NTR6727

Register	ID
CCMO	NL6349.018.17 - ABR

Resultaten

Samenvatting resultaten

Vijverberg SJ, Pijnenburg MW, Hövels AM, Koppelman GH, Maitland-van der Zee AH. The need for precision medicine clinical trials in childhood asthma: rationale and design of the PUFFIN trial. Pharmacogenomics. 2017;18(4):393-401.