Pharmacogenetics Use For Further treatment Improvement in childreN

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21847

Source
NTR

Brief title
PUFFIN

Health condition

Uncontrolled asthma, LABA response heterogeneity

Ongecontroleerd astma, LABA respons heterogeniteit

Sponsors and support

Primary sponsor: Academic Medical Center (AMC)
Source(s) of monetary or material Support: Longfonds

Intervention

Outcome measures

Primary outcome

Improvement of asthma control based on repeated measurement analysis of (childhood)-

Asthma Control Test after 3 months

Secondary outcome

- Improvement of asthma control based on repeated measurement analysis of (childhood)-Asthma Control Test after 6 months

- time to ACT >= 20

- change in asthma-related quality of life scores

- change in fatigue score

- school absences

- exacerbations (oral corticosteroids use, ER visits, hospital admissions)

- time to first exacerbation

- amount of changes in therapy at t=3 months

- change in lung function (FEV1 pre- and postbronchodilator) at t=3 and t=6 months

- change in FeNO at t=3 and t=6 months

- change in nasal gene expression and nasal gene methylation in relation to the treatment effect at t=3 and t=6 months

- Incremental cost per Quality Adjusted Life Year (QALY)

- Incremental costs per avoided exacerbation

Study description

Background summary

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.

Study objective

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

Study design

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

Intervention

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.

Contacts

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Eligibility criteria

Inclusion criteria

- 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

Exclusion criteria

- 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

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2018
Enrollment:	310
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6539
NTR-old	NTR6727
CCMO	NL6349.018.17 - ABR

Study results

Summary results
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.