Pharmacogenetics Use For Further treatment Improvement in childreN

Published: 21-12-2017
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To assess whether ADRB2 genotype-guided asthma treatment in children with persistend athma symptoms despite ICS treatment leads to better asthma control compared to non-genotype-guided asthma treatment.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON55682

Source
ToetsingOnline

Brief title
PUFFIN

Condition

- Allergic conditions
- Bronchial disorders (excl neoplasms)

Synonym
Asthma, chronic airway obstruction

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Longfonds

Intervention

Keyword: ADRB2 polymorphism, Childhood Asthma, long-acting beta2-agonists, Pharmacogenetics

Outcome measures

Primary outcome

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

Secondary outcome

Change in asthma control score at t=6 months, time to ACT >= 20 (continuous variable), 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, change in FeNO at t=3 and t=6.

Study description

Background summary

Asthma is the most chronic disease in children. There is a large variability in treatment response to asthma medication and a one-size fits all approach might not be optimal for all paediatric patients. In children who are not well controlled on inhaled corticosteroïds (ICS), guidelines suggest to double the dose of ICS or add a long acting beta-agonist (LABA). Variation in the gene encoding the beta2 adrenergic receptor (ADRB2), has been associated in multiple paediatric asthma populations with poor response to long-acting beta2 agonists (LABA). Paediatric asthma patients carrying the risk variant might therefore benefint more from doubling ICS dosages than from receiving LABAs.

Study objective

To assess whether ADRB2 genotype-guided asthma treatment in children with

persistend athma symptoms despite ICS treatment leads to better asthma control compared to non-genotype-guided asthma treatment.

Study design

Dutch national, multi-centre randomized controlled double blind trial

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 receive LABA. In the usual care arm, children will be randomized between doubling ICS dosage or LABA treatment, the two most common chosen options among respiratory paediatricians in the Netherlands when children are uncontrolled despite low dosages of ICS.

Study burden and risks

Risks: nasal swabbing (soft tip swabs, Copan) provides a minimal burden to the children, as is the donation of saliva and feces. Repeated lung function measurements can be experienced as uncomfortable in case of spirometer induced bronchoconstriction, which happens <3% in asthmatic children. We will monitor this with repeated lung function measurements, and administer salbutamol 400 mcg if needed (pMDI with spacer). Furthermore, there are no risks for the participation in the study. The risks associated with participation can be considered negligible and the burden minimal.

This study includes minors, since the effect of the ADRB2 genotype on response to asthma medication seems to be restricted to the paediatric population. This patient group is expected to have the most benefit from prospective ADRB2 genotyping before starting treatment.

Benefits: chirldren may be more fastly controlled when genotyping results to the best medication for the individual child.

We will set up a patient panel to assure that the intrests of the patients will be served.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- Between 6-18 years of age
- Doctor's diagnosis of asthma based on patient history, 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 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
- LABA use in the past 6 months
- omalizumab use
- ICU admission in the previous year

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-06-2018
Enrollment:	300
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Inhaled Corticosteroïds (ICS)
Generic name:	n.v.t.
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Long Acting Beta2 Agonists (LABA)
Generic name:	n.v.t.
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-12-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-09-2019

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-09-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	6727
EudraCT	EUCTR2017-004424-29-NL
CCMO	NL63849.018.17

Study results

Date completed: 01-11-2023

Actual enrolment: 100

Summary results
Trial is onging in other countries