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A precision medicine trial to study heterogeneity in pediatric asthma: design of the PUFFIN trial
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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 [1,2].

The aim is 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.

Methods
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 (figure 1). Lung function measurements, questionnaires focussing on asthma control (ACT/c-ACT) and quality of life, will be obtained in three visits within 6 months.

Results
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 [3].

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

References
3. Vijverberg SJH, 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. 18(4), 393-401 (2017).

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