Introduction
Inhaled corticosteroids (ICS) are the most commonly prescribed medication to control persistent asthma. However, a high proportion of patients does not respond to this medication and suffer exacerbations. Genetic variation has shown to influence treatment response to ICS. In this study we aim to identify genetic variants associated with asthma exacerbations despite ICS use in European children.

Methods
Within the Pharmacogenomics in Childhood Asthma (PiCA) consortium we performed a Genome-Wide Association Study (GWAS) of asthma exacerbations in 3 European cohorts; PACMAN (NL), PASS (UK), and followMAGICS (GER). In total, 1,204 asthmatic children treated with ICS were analysed. Imputation of genetic variants was performed using the Haplotype Reference Consortium as reference panel by means of the Michigan Imputation Server. Association testing of 7.5 million genetic variants with minor allele frequency ≥1% was performed using logistic regression models with EPACTS. Subsequently, results were meta-analyzed using METASOFT.
**Results**

A total of 74 genetic variants were suggestively associated with asthma exacerbations despite the use of ICS ($p\leq 5\times 10^{-6}$). The most significant variants were located in 9 different loci (minimum $p$-value=$2.3\times 10^{-7}$), including one gene previously identified as associated with ICS response in Asian populations ($ALLC$). Additionally, novel associations were revealed in biologically plausible genes with drug metabolism functions and in genes belonging to the Wnt/β-catenin signaling pathway.

**Conclusion**

This is the first GWAS of ICS response in European children with asthma. We identified several novel genes suggestively associated with asthma exacerbations despite the use of ICS. These results will be validated with further independent studies.

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