European Respiratory Society
Annual Congress 2012

Abstract Number: 7164

Publication Number: P469

Abstract Group: 12.3. Genetics and Genomics

Keyword 1: Asthma - management **Keyword 2:** Genetics **Keyword 3:** Biomarkers

Title: GLCCI1 rs37972 gene's polymorphism correlation with response to oral glucocorticosteroids treatment in severe asthmatics from the BIOAIR cohort

Maciej 1244 Kupczyk maciek.kupczyk@ki.se MD [1], Lovisa 1245 Reinius lovisa.reinius@ki.se [2], Roelinde 1246 Middelvleld roelinde.middelveld@ki.se [1], Barbro 1247 Dahlen barbro.dahlen@ki.se MD [1], Juha 1248 Kere juha.kere@ki.se [2] and Sven-Erik 1249 Dahlen sven-erik.dahlen@ki.se MD [1]. [1] EAAF, IMM, Karolinska Institutet, Stockholm, Sweden and [2] Departament of Biosciences and Nutrition, Karolinska Institutet, Stockholm, Sweden .

Body: A significant association of SNP rs37972 in GLCCI1 in a genomewide study was identified in children with asthma. Our goal was to evaluate biomarkers and pharmacogenetic determinants that may improve effectiveness of treatment in adults with SA. Eighty five SA patients and 66 with mild-to-moderate asthma (MA) were included in the BIOAIR study. After optimization of treatment, they underwent a double-blind 2 week oral steroid intervention (prednisolone 0.5 mg/kg/day). DNA was extracted from whole blood and the rs37972 (C/T) polymorphism in the GLCCI1 gene was analyzed using TaqMan allelic discrimination on the ABI Prism 7500 detection system. The oral steroid intervention resulted in a significant increase in FEV1 (% predicted) in SA (6.6%, 95% CI 2.4 – 10.8, p=0.002, steroid treatment vs placebo) but not in MA (-0.5%, 95% CI -3.4 – 2.4, p=0.38) or COPD (1.2%, 95% CI -1.7 – 4.0, p=0.35)(p=0.02,between group comparisons). The responsiveness to oral steroids was significantly better in patients characterized by the highest blood eosinophils (>0.44x109/L), the highest sputum eosinophils (>4%), the lowest sputum neutrophils (<49%) and the highest FeNO (>40ppb). A functional GLCCI1 variant was weakly associated with reduced improvement of lung function in response to glucocorticosteroids (p>0.05) and correlated significantly with the number of eosinophils in induced sputum and FeNO (p<0.05). In the majority of SA patients, systemic steroid treatment induces an improvement in lung function. The positive response to oral steroids may be associated with certain genotype and phenotypic markers that may improove therapeutic decisions.