

European Respiratory Society Annual Congress 2013

Abstract Number: 2977

Publication Number: P3142

Abstract Group: 5.3. Allergy and Immunology

Keyword 1: Asthma - diagnosis **Keyword 2:** Biomarkers **Keyword 3:** Inflammation

Title: Associated factors with persistent airflow limitation in asthma in U-BIOPRED

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Body: Rationale Current therapeutic options fail to prevent or reverse irreversible obstruction in some patients with asthma. Careful phenotyping will allow more detailed understanding of the underlying pathophysiology, such as the accompanying inflammatory pathways. This can promote the development of targeted prophylaxis or treatment. Aim To examine whether fixed airways obstruction in patients with asthma is associated with markers of airway inflammation, FeNO, total IgE, and BMI. Methods This was a cross-sectional analysis of the U-BIOPRED cohort. Severe asthma was defined by the IMI-criteria (Bel et al. Thorax 2011). Patients with mild/moderate asthma used ICS (≤ 500 mcg FP), were (partly) controlled according to GINA-criteria, and were (ex)non-smokers (≤ 5 py). Fixed airways obstruction was defined as a postbronchodilator FEV₁ or FEV1/FVC < 75% predicted with a TLC > 75% predicted. Wilcoxon rank sum test was used to test for associating factors. Results Data were available for 148 patients, of which 118 with severe asthma. Persistent airflow limitation was observed in 46% of the patients and was significantly associated with sputum eosinophils (Sp.eos.), sputum alveolar macrophages (Sp.alv.macroph.) and age (Table 1).

Table 1

| | Fixed airflow obstruction | Control | p-value |
|----------------------------|----------------------------------|------------------|----------------|
| Age* | 55.3 (11.7) | 46.8 (15.2) | 0.0006 |
| Sp.alv.macroph.(%)† | 24.8 (13.2-37.7) | 40.6 (27.4-65.3) | 0.01 |
| Sp.eos.(%)† | 12.3 (2-34.3) | 1.88 (0.2-11.1) | 0.03 |

*mean(standard deviation) ; †median(interquartile range)

Conclusion This preliminary analysis of the U-BIOPRED cohort shows that fixed airflow limitation in asthma is associated with elevated sputum eosinophils and lower sputum alveolar macrophages, suggesting a distinguishable inflammatory profile in the airways.