Exhaled breath profiling and eosinophilic airway inflammation in asthma – results of a pilot study

Rationale
Eosinophilic inflammation in asthma is predictive for responses to inhaled steroids. The application of sputum analysis is limited by requirements of lab facilities and not-directly available results. Exhaled air metabolomic profiles are associated with eosinophilic inflammation in asthma (Ibrahim et al. Thorax 2011; 66(9): 804-9). We hypothesized that breathprint profiles analysed by electronic noses (eNoses) can be surrogate markers for eosinophilic airway inflammation.

Aim
To test whether breathprints analysed by the multiple sensors in the eNose-platform from U-BIOPRED can discriminate eosinophilic asthma from non-eosinophilic asthma.

Methods
Breath samples from a subset of patients (>18yr) with mild/moderate/severe asthma included in the U-BIOPRED study were analysed by 158 sensors from four different types of eNoses using: 1) carbon-polymer sensors, 2) quartz microbalance metalloporphyrins sensors, 3) metal oxide semiconductor sensors, and 4) field asymmetric ion mobility spectrometry. Asthma diagnosis was based on a history of wheeze with reversibility of ≥12%/200ml in FEV₁ after 400mcg salbutamol OR airway hyper-responsiveness (PC₂₀ <8 mg/ml) OR diurnal PEF variation OR a decrease in FEV₁ within four weeks after treatment tapering. All patients with mild/moderate asthma used inhaled corticosteroids (≤500mcg FP), were (partly)controlled according to GINA-criteria, and were non-smokers or ex-smokers (≤5 py). Severe asthma was based on the IMI-criteria (Bel et al. Thorax 2011; 66(10): 910-7).

Induced sputum processing was done by selected plug method and differential cell counts were measured. Breathprints were analysed by discriminant analysis on all significant associated sensors, resulting in cross-validated accuracy values and a bootstrap based ROC-curve.

Results
Complete data on sputum and exhaled breath samples were available for 27 patients: 25 patients with severe asthma and two patients with mild/moderate asthma. Nineteen patients had sputum eosinophilia (i.e. eosinophils >3%). Eight significantly associated sensors were able to discriminate breathprints from patients with eosinophilic or non-eosinophilic asthma with 85% accuracy, and an ROC-area under the curve of 99% (95% CI: 0.9752-1) (Figure 1).

Conclusion
These preliminary data show that eNose breathprints can distinguish between eosinophilic and non-eosinophilic asthma. This suggests that eNoses may have a potential for subphenotyping of asthma patients using an easily applied method that is even less invasive than induced sputum. This could be used for patient selection drug trials targeting eosinophilic or non-eosinophilic endotypes. The inclusion of patients will continue, to validate/confirm these results in a larger sample-size.

Funded by IMI

Word count: 383 (max 400)
Figure 1. ROC-curve with 95% confidence interval for the diagnosis of eosinophilic asthma compared to non-eosinophilic asthma (AUC 0.993).