Association of sputum and blood eosinophil concentrations with clinical measures of COPD severity: an analysis of the SPIROMICS cohort

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Summary

Background Increased concentrations of eosinophils in blood and sputum in chronic obstructive pulmonary disease (COPD) have been associated with increased frequency of exacerbations, reduced lung function, and corticosteroid responsiveness. We aimed to assess whether high eosinophil concentrations in either sputum or blood are associated with a severe COPD phenotype, including greater exacerbation frequency, and whether blood eosinophils are predictive of sputum eosinophils.

Methods We did a multicentre observational study analysing comprehensive baseline data from SPIROMICS in patients with COPD aged 40–80 years who had a smoking history of at least 20 pack-years, recruited from six clinical sites and additional subsites in the USA between Nov 12, 2010, and April 21, 2015. Inclusion criteria for this analysis were SPIROMICS baseline visit data with complete blood cell counts and, in a subset, acceptable sputum counts. We stratified patients on the basis of blood and sputum eosinophil concentrations and compared their demographic characteristics, as well as results from questionnaires, clinical assessments, and quantitative CT (QCT). We also analysed whether blood eosinophil concentrations reliably predicted sputum eosinophil concentrations. This study is registered with ClinicalTrials.gov (NCT01969344).

Findings Of the 2737 patients recruited to SPIROMICS, 2499 patients were smokers and had available blood counts, and so were stratified by mean blood eosinophil count: 1262 patients with low (<200 cells per μL) and 1237 with high (≥200 cells per μL) blood eosinophil counts. 827 patients were eligible for stratification by mean sputum eosinophil percentage: 656 with low (<1·25%) and 171 with high (≥1·25%) sputum eosinophil percentages. The high sputum eosinophil group had significantly lower median FEV1 percentage predicted than the low sputum eosinophil group both before (65·7% [IQR 51·8–81·3] vs 75·7% [59·3–90·2], p<0·0001) and after (77·3% [63·1–88·5] vs 82·9% [67·8–95·9], p=0·001) bronchodilation. QCT density measures for emphysema and air trapping were significantly higher in the high sputum eosinophil group than the low sputum eosinophil group. Exacerbations requiring corticosteroids treatment were more common in the high versus low sputum eosinophil group (p=0·002). FEV1 percentage predicted was significantly different between low and high blood eosinophil groups, but differences were less than those observed between the sputum groups. The high blood eosinophil group had slightly increased airway wall thickness (0·02 mm difference, p=0·032), higher St George Respiratory Questionnaire symptom scores

(p=0·037), and increased wheezing (p=0·018), but no evidence of an association with COPD exacerbations (p=0·35) or the other indices of COPD severity, such as emphysema measured by CT density, COPD assessment test scores, Body-mass index, airflow Obstruction, Dyspnea, and Exercise index, or Global Initiative for Chronic Obstructive Lung Disease stage. Blood eosinophil counts showed a weak but significant association with sputum eosinophil counts (receiver operating characteristic area under the curve of 0·64, p<0·0001), but with a high false-discovery rate of 72%.

Interpretation In a large, well characterised cohort of former and current smoking patients with a broad range of COPD severity, high concentrations of sputum eosinophils were a better biomarker than high concentrations of blood eosinophils to identify a patient subgroup with more severe disease, more frequent exacerbations, and increased emphysema by QCT. Blood eosinophils alone were not a reliable biomarker for COPD severity or exacerbations, or for sputum eosinophils. Clinical trials targeting eosinophilic inflammation in COPD should consider assessing sputum eosinophils.

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