Systemic effects of fluticasone on blood eosinophils in bronchiectasis

To the Editor:

We read with interest the observations of Aliberti *et al.* [1] showing that blood eosinophilia predicts the quality of life response to inhaled fluticasone propionate (FP) in bronchiectasis, apparently independently of concomitant asthma or COPD. Pointedly they only appeared to have measured blood eosinophils at baseline and not during treatment with FP. This is pertinent as FP produces dose-dependent suppression of blood eosinophils due to systemic absorption from the lung. Hence, 1 mg of inhaled fluticasone in asthma patients is systemically equivalent to 5.3 mg of oral prednisolone for blood eosinophil suppression and 8.5 mg for cortisol suppression [2]. We would therefore be interested to know if similar improvements in quality of life occur in bronchiectasis in relation to blood eosinophilia with other inhaled corticosteroids (ICS) that exhibit much less systemic glucocorticoid potency, such as budesonide or beclmomethasone [3]. Also, it would be interesting to know if patients with bronchiectasis who have other elevated type-2 biomarkers, such as fractional exhaled nitric oxide, might also benefit from either inhaled FP or other ICS [4].

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Fluticasone response in bronchiectasis may be explained by its systemic eosinophil suppression https://bit.ly/3dDd74E

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Blood eosinophils do not predict inhaled budesonide response in bronchiectasis

From the authors:

We would like to thank B. Lipworth and co-workers for their feedback on our study, which showed that 6-month treatment with inhaled fluticasone proprionate (FP) significantly improved quality of life in bronchiectasis patients with neither asthma nor COPD, and with blood eosinophil counts either ⩾3% or⩾150 cells·μL^{-1} [1, 2]. We agree with B. Lipworth and co-workers on the higher dose-dependent suppression of blood eosinophils due to the systemic absorption of FP. We re-analysed previously published data on bronchiectasis patients treated with budesonide, which has less systemic potency than FP [3]. We carried out a *post hoc* analysis of a randomised, double-blind, parallel-group trial, which enrolled 40 bronchiectasis patients (excluding those with COPD or asthma) who underwent a total of 6-month treatment with budesonide: 20 patients underwent 3 months of 1600 μg daily and, then, 3 months of high dose of budesonide (1600 μg daily), whereas 20 patients underwent 3 months of 1600 μg daily and, then, a low dose of budesonide (640 μg) plus 9 μg of formoterol. At baseline, median (interquartile range (IQR)) percentage of blood eosinophil counts was 2.8% (2.0–4.1%) and median (IQR) Saint George's Respiratory Questionnaire (SGRQ) value was 38.1 (20.3–56). 38.4% showed an improved quality of life defined by a decreased SGRQ (at least 4 points). No significant differences were found in the median (IQR) percentage of blood eosinophil count at baseline between those who improved (⩾4 points in the SGRQ) and those who did not improve their quality of life: 3.1% (2.1–4.4%) *versus* 2.5% (1.9–3.6%), respectively ($p=0.449$). Furthermore, quality of life before and after 6 months of treatment did not change when the sample was stratified using cut-offs of 3% and 150 cells·μL^{-1} of blood eosinophils at baseline (table 1). Unfortunately, data on exhaled nitric oxide fraction were not collected [2, 3]. Although a control group was not recruited and the statistical power was poor, our results seem to support the hypothesis of B. Lipworth and co-workers that a 6-month therapy with budesonide does not improve quality of life in pure bronchiectasis patients without asthma or COPD and with blood eosinophilia (⩾3% or ⩾150 cells·μL^{-1}). Finally, the repeatability of eosinophil count over time is another interesting point raised by B. Lipworth and co-workers. A moderate/good concordance of peripheral eosinophil counts (intraclass correlation coefficient (ICC) 0.6) was found from baseline to 12 weeks of follow up in a trial of 86

TABLE 1 Changes in Saint George's Respiratory Questionnaire (SGRQ) comparing low (LowEos) and high eosinophil group patients (HighEos) (cut-off points of 3% and 150 cells·μL^{-1})

Variable (n=40)	LowEos Group (Eos <3%) n=23 (57.5%)	HighEos Group (Eos ⩾3%) n=17 (42.5%)	p-value	LowEos Group (Eos <150) n=26 (65%)	HighEos Group (Eos ⩾150) n=14 (35%)	p-value
Baseline SGRQ	38.4 (16.7 to 57.5)	38.9 (20.5 to 51.6)	0.847	37.7 (17.4 to 57.5)	39.4 (18.1 to 52.7)	0.885
Change SGRQ ⩾4 points %	36.4%	41.2%	0.509	36%	42.9%	0.466
SGRQ total change	−0.8 (−7.4 to 9.9)	−2.9 (−8.4 to 7.7)	0.489	−0.9 (−8.1 to 9.6)	−2.9 (−7.9 to 8.1)	0.408

Data are presented as median (interquartile range), unless otherwise stated.

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bronchiectasis patients exposed to FP [4]. However, ICC decreased to 0.4 after 24 weeks of follow-up. Moreover, the results did not change administration of moderate (250 µg twice daily) or high dose (500 µg twice daily) of FP. In conclusion, if our preliminary data were to be confirmed by well-designed randomised controlled trials recruiting bronchiectasis patients with blood eosinophilia exposed to FP *versus* budesonide *versus* other inhaled corticosteroids, the use of inhaled corticosteroids in the bronchiectasis population will have key clinical implications.

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