

Correspondence

Biomarkers to predict inhaled corticosteroid response

To the Editor:

The article by Cowan et al¹ looked at the relationship between T_H2 biomarkers and inhaled corticosteroid (ICS) response over 4 weeks, defined as significant improvements in the Asthma Control Questionnaire (ACQ) score, FEV₁, and PC₂₀AMP in 30 patients with eosinophilic asthma. There are several methodological aspects of the study that may have influenced their results. The choice of AMP for indirect bronchial challenge testing was presumably due to it being more sensitive to ICS compared with the more conventional direct-acting methacholine.^{2,3} Hence, one might not have seen as many ICS responders had methacholine been used instead of AMP. It would also be relevant to know the proportion of patients who ended up with a well-controlled absolute ACQ score of less than 0.75 rather than a change of more than 0.5 in the ACQ score after treatment with ICS. The chosen dose (ex-valve) of fluticasone propionate was rather high at 1000 µg/d, which in real life would be an unlikely starting dose for such patients. Indeed, it has been shown that 1000 µg/d (ie, 440 µg twice a day ex-actuator dose) of inhaled fluticasone propionate leads to systemic corticosteroid activity equivalent to that induced by 8.5 mg/d (95% CI, 5.7-11.2 mg) of oral prednisolone in terms of comparable cortisol suppression in patients with asthma.⁴ Thus, one may not be able to extrapolate the present biomarker results to what happens with more conventional lower starting doses of ICS devoid of systemic corticosteroid activity. Finally, when inspecting the odds ratios for ICS response with respect to baseline sputum eosinophil levels of

more than 3%, very wide 95% CI of 2.31 to 43.09 and 1.73 to 203.7 were revealed for improvements in 2 or 3 clinical outcomes, respectively, with the corresponding 95% CI for exhaled nitric oxide (>35 ppb) being 0.93 to 413.54 and 1.73 to 203.7, in turn, suggesting that such tests are much too variable to be used in everyday practice.

Brian J. Lipworth, MD

From the Scottish Centre for Respiratory Research, Ninewells Hospital and Medical School, University of Dundee, Dundee, United Kingdom. E-mail: bj.lipworth@dundee.ac.uk.

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REFERENCES

1. Cowan DC, Taylor DR, Peterson LE, Cowan JO, Palmay R, Williamson A, et al. Biomarker-based asthma phenotypes of corticosteroid response. *J Allergy Clin Immunol* 2015;135:877-83.e1.
2. Wilson AM, Lipworth BJ. Dose-response evaluation of the therapeutic index for inhaled budesonide in patients with mild-to-moderate asthma. *Am J Med* 2000; 108:269-75.
3. Dempsey O, Kennedy G, Lipworth B. Comparative efficacy and anti-inflammatory profile of once-daily therapy with leukotriene antagonist or low-dose inhaled corticosteroid in patients with mild persistent asthma. *J Allergy Clin Immunol* 2002;109:68-74.
4. Wilson AM, Lipworth BJ. Short-term dose-response relationships for the relative systemic effects of oral prednisolone and inhaled fluticasone in asthmatic adults. *Br J Clin Pharmacol* 1999;48:579-85.

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