



## Letters to the Editor

### Inhaled Corticosteroids, Eosinophils and Chronic Obstructive Pulmonary Disease Exacerbations\*

### Corticoides inhalados, eosinófilos y exacerbaciones de la enfermedad pulmonar obstructiva crónica

To the Editor,

In a recent edition of ARCHIVOS DE BRONCONEUMOLOGÍA, Baloira Villar et al. discussed the consensus on the use of inhaled corticosteroids (ICS) in chronic obstructive pulmonary disease (COPD), and made some interesting comments.<sup>1</sup> In line with other authors, they suggest, in their last paragraph, that eosinophilia is currently the best marker for ICS response in COPD. However, we believe that some clarification is necessary.

It is true that, at the moment, eosinophilia in sputum appears to be the most reliable predictor of therapeutic response, but it is a technically complex test that can only be performed in a few hospitals in Spain, so is of little general use. Several recent studies have evaluated the possibility of using blood eosinophilia as more accessible biomarker for predicting response to the combination of long-acting beta-agonists (LABA) and ICS in COPD in terms of reducing exacerbations. This marker appears to have an acceptable correlation with sputum eosinophilia, and results have been promising. The most commonly used cut-off point is  $\geq 2\%$  eosinophils. However, practically all these reports consist of *post hoc* analyses of clinical trials in which the evaluation of eosinophilia and its relationship with therapeutic response was not an initial study objective, so these results must be viewed with caution.<sup>2</sup> The relationship between blood eosinophilia and the risk of exacerbation has not yet been clarified, nor has the best cut-off point for eosinophils been determined. In a recent article, eosinophil levels  $\geq 2\%$  predicted severe exacerbations in COPD patients, but paradoxically, the rate of moderate exacerbations was lower in patients with eosinophil values above this limit.<sup>3</sup> However, a different measurement (340 eosinophils/ $\mu$ l) showed that patients who exceeded these values developed more moderate and severe exacerbations.<sup>3</sup> It is thus difficult at present to apply these findings in clinical practice.

Furthermore, the analytical tests used in the clinical trials cited were based on blood eosinophil levels determined at the time



of patient recruitment to predict exacerbations in the immediate post-test period, which can vary widely, while a study derived from the ECLIPSE cohort showed that 49% of patients had eosinophil counts ranging above and below 2% throughout the study.<sup>4</sup> This raises new questions for clinicians, such as the possibility that ICS might (or must) be withdrawn or reinitiated during follow-up, depending on the evolution of eosinophil levels. Such questions can only be answered with specifically designed studies addressing these issues.

In summary, blood eosinophilia is a promising biomarker in COPD, but we are far from being able to use it to safely determine treatment for stable-phase COPD, and it seems likely that in the future it will be combined with other markers, such as periostin.<sup>5</sup> We agree with Baloira Villar et al. in their final conclusion: COPD is a highly heterogenic disease, and more biomarkers are needed to help us tailor treatment.

## References

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Rafael Golpe,\* Irene Martín-Robles, Pilar Sanjuán-López

Servicio de Neumología, Hospital Universitario Lucus Augusti, Lugo, Spain

\* Corresponding author.

E-mail address: [rafagolpe@gmail.com](mailto:rafagolpe@gmail.com) (R. Golpe).

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