

## Correspondence

## Reply

To the Editor:

We appreciate the feedback from Sinico et al<sup>1</sup> regarding our recent article on the relationship between antineutrophil cytoplasmic autoantibody (ANCA) status and the clinical phenotypes of Churg-Strauss syndrome (CSS).<sup>2</sup> We would like to acknowledge at the outset the contribution of Sinico et al<sup>1</sup> in this area of research.

As Sinico et al<sup>1</sup> point out in their letter, our study findings substantially agreed with both their findings and those of Sablé-Froutassau et al<sup>3</sup> regarding the frequency that ANCAs are found in patients with CSS and also the clinical phenotypes that are associated with ANCA status. Our approach was novel by undertaking an analysis of the US Food and Drug Administration's adverse events database as opposed to a traditionally collected case series. It is interesting that there was agreement despite our data being derived from multiple different reporting clinicians and presumably multiple different testing platforms/slides/substrates for both ANCA indirect immunofluorescence (IIF) and the confirmatory detection methods for anti-myeloperoxidase (MPO)/anti-proteinase 3 (PR3) antibodies. Other authors have reported significant variation in the performance of anti-MPO antibody ELISAs when assessed against clinically relevant samples.<sup>4</sup>

We acknowledge that our statement that "this is the only case series investigating the clinical expression of CSS in relation to ANCA status in which a positive IIF assay result required confirmation by using ELISA" requires clarification.<sup>2</sup> The intent of this statement was to highlight an important difference in the analysis we carried out compared with previous studies. Previous studies, including those of Sinico et al,<sup>3,5</sup> did perform anti-MPO and anti-PR3 confirmatory testing; however, our understanding of their studies is that the analysis was based on ANCA positivity, as assessed by means of IIF. Our study analysis was based on whether the patient had positive anti-MPO results. As stated in our discussion, the reason for this approach is that both with IIF classical and atypical ANCA patterns, there are many other potential antigenic specificities apart from MPO and PR3 that can lead to an ANCA pattern. Most of these other specificities have not conclusively been shown from a diagnostic perspective to indicate the presence of vasculitis. We therefore concluded that restricting our analysis to anti-MPO-positive versus

ANCA-negative results was more likely to appropriately segregate the subgroups in a clinically meaningful way.

We note with interest the 2 different mechanisms proposed in both ANCA-negative and ANCA-positive peripheral neuropathy in patients with CSS by Oka et al.<sup>6</sup> We hope that the associations highlighted by our and previous studies continue to provide pathways by which the underlying pathogenic mechanisms of disease can be further elucidated.

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## REFERENCES

1. Sinico RA, Bottero P, Guillemin L. Antineutrophil cytoplasmic autoantibodies and clinical phenotype in patients with Churg-Strauss syndrome. *J Allergy Clin Immunol* 2012;XXX:XXX-X.
2. Healy B, Bibby S, Steele R, Weatherall M, Nelson H, Beasley R. Antineutrophil cytoplasmic autoantibodies and myeloperoxidase autoantibodies in clinical expression of Churg-Strauss syndrome. *J Allergy Clin Immunol* 2012 [in press].
3. Sablé-Froutassau R, Cohen P, Mahr A, Pagnoux C, Mouthon L, Jayne D, et al. Antineutrophil cytoplasmic antibodies and the Churg-Strauss Syndrome. *Ann Intern Med* 2005;143:632-8.
4. Trevisin M, Pollock W, Dimech W, Melny J, Paspaliaris B, Gillis D, et al. Antigen-specific ANCA ELISAs have different sensitivities for active and treated vasculitis and for nonvasculitic disease. *Am J Clin Pathol* 2008;129:42-53.
5. Sinico RA, Di Toma L, Maggiore U, Bottero P, Radice A, Tosoni C, et al. Prevalence and clinical significance of antineutrophil cytoplasmic antibodies in Churg-Strauss syndrome. *Arthritis Rheum* 2005;52:2926-35.
6. Oka N, Kawasaki T, Matsui M, Shigematsu K, Unuma T, Sugiyama H. Two subtypes of Churg-Strauss syndrome with neuropathy: the roles of eosinophils and ANCA. *Mod Rheumatol* 2011;21:290-5.

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