

Correspondence

Mepolizumab response in severe chronic rhinosinusitis with nasal polyps is dissociated from blood eosinophil levels

To the Editor:

Clinicians who manage patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP) now have the choice of using licensed biologics, including mepolizumab, dupilumab, and omalizumab.¹ One might expect the response to such biologics to be determined by type 2 biomarkers such as peripheral blood eosinophils (PBEs), as is the case with asthma. Indeed, patients who have asthma and comorbid CRSwNP have higher levels of type 2 inflammatory biomarkers, including PBE, than do patients with asthma alone.²

We were therefore intrigued to read the *post hoc* analysis of the SYNAPSE trial in severe CRSwNP, in which the clinical response to mepolizumab was not determined by baseline PBE levels for the coprimary end points of endoscopic nasal polyp score (NPS) and nasal obstruction visual analog scale.³ For example the proportion of patients with at least a 1-point improvement in nasal polyp score for the difference between mepolizumab and placebo was 21.7% for patients with a PBE level less than 300 cells/ μ L compared with 22.3% for patients with a PBE level of at least 300 cells/ μ L.

For the key secondary end point of rescue surgical polypectomy, a significant reduction was observed with mepolizumab in patients with a baseline PBE level of at least 300 cells/ μ L but not with a PBE level less than 300 cells/ μ L, although the CIs for the hazard ratios were widely overlapping. Similar findings were reported in relation to the need for rescue medical polypectomy with oral corticosteroids. We appreciate that the power of *post hoc* analysis can be confounded by smaller numbers according to subgroups of patients.

Nonetheless, the observation that the clinical efficacy of mepolizumab appears to be dissociated from PBE level is rather counterintuitive given that its mechanism of action is via eosinophil suppression. In turn, the inference here is that mepolizumab is equally efficacious in patients with type 2 low CRSwNP, at least in regard to PBE levels, whereas in asthma the opposite applies.⁴ We would welcome real-life pragmatic trials to assess the relative efficacy of mepolizumab in patients with

asthma and CRSwNP⁵—in particular, trials looking at the differential response according to PBE level in the upper and lower airway.

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Editor's note: There is no accompanying reply to this correspondence.

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