

Correspondence

Eosinophil paradox with mepolizumab in chronic rhinosinusitis with nasal polyposis



To the Editor:

We were intrigued to read the *post hoc* analysis by Howarth et al¹ suggesting that 100 mg mepolizumab given subcutaneously may reduce disease burden in the upper and lower airways of patients with severe eosinophilic asthma and chronic rhinosinusitis with nasal polyposis (CRSwNP). Pointedly, the diagnosis of CRSwNP was not based on either sinonasal endoscopy or computed tomography scan. The subgroup of patients in the MUSCA trial who completed the 22-item Sino-Nasal Outcome Test (SNOT-22) exhibited a mean treatment effect of -11.8 with mepolizumab, which exceeded the minimal clinically important difference of -8.9 . To put this magnitude of change with mepolizumab into context, mean changes of -21.2 and -17.8 in SNOT-22 score were seen in 2 trials with dupilumab in patients with properly documented CRSwNP.²

In support of the effectiveness of mepolizumab in the upper airway, Howarth et al cite a trial where 750 mg mepolizumab given intravenously significantly reduced the need for the surgery, while another study using the same 750 mg intravenous dose of mepolizumab also showed a significant reduction in endoscopic nasal polyp score. We have reported a series of patients with severe eosinophilic asthma in whom mepolizumab given subcutaneously improved asthma control while suppressing blood eosinophils from a mean of 1393 to 120 cells/ μL .³ In contrast, in these patients with a mean baseline Lund-Mackay score of 21/24, mepolizumab had no impact on CRSwNP exacerbations requiring corticosteroids, endoscopic nasal polyp score, or persistent anosmia. Indeed, Laidlaw et al⁴ reported a disconnect between depletion of blood and tissue eosinophils with dexamipexole over 6 months with no change in polyp size or improvement in symptoms.⁴

Hence, we remain unconvinced that mepolizumab at the recommended subcutaneous dose of 100 mg is effective for the treatment of concomitant eosinophilic CRSwNP despite improvements in asthma control and reductions in eosinophils. In particular, we await with interest the results of the completed trial with mepolizumab in CRSwNP using the 100 mg subcutaneous dose (NCT03085797) to confirm or refute whether there may be dissociation in effects between endoscopic nasal polyp and SNOT-22 scores.

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Reply



To the Editor:

We thank Lipworth et al¹ for their correspondence about our recent publication,² within which they acknowledge that studies with mepolizumab in chronic rhinosinusitis with nasal polyposis (CRSwNP) have shown benefit in reducing nasal polyp size.^{3,4} They, however, question the 22-item Sino-Nasal Outcome Test (SNOT-22) findings from the MUSCA⁵ study, a placebo-controlled study of mepolizumab in 551 participants with severe eosinophilic asthma of whom 19% (n = 105) reported nasal polyps at screening. The analysis of the SNOT-22 outcome found that mepolizumab significantly improved this upper airway outcome measure compared with placebo in those with this history of CRSwNP. The improvement with mepolizumab exceeded the recognized minimally important difference for SNOT-22, identifying the clinical relevance of this effect. Such an improvement was not seen with mepolizumab in those participating in the MUSCA study who did not report nasal polyps at screening, identifying the relevance of the CRSwNP findings. Lipworth et al questioned the findings, because this did not concord with their personal experience with mepolizumab in 6 patients.⁶ We are sure, however, that the authors would not contest that a large prospective formally conducted placebo-controlled clinical trial is more substantial than an anecdotal case report. Nevertheless, they reported a disparity of effect with mepolizumab within the upper and lower airways in their subjects. Mepolizumab, as an mAb that targets IL-5, is specific in targeting eosinophilic inflammation. Although most nasal polyps are eosinophilic in Europe and the United States, not all are and there is a diversity of pathology. Those that are noneosinophilic would not be expected to respond to therapeutic intervention with mepolizumab. Indeed, in the previous