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## Blood eosinophil counts predict treatment response in patients with severe eosinophilic asthma

To the Editor:

In a letter to the editor published in the March 2015 issue of the *Journal*, Fowler et al<sup>1</sup> found that a blood eosinophil cutoff of 150 cells/ $\mu$ L had a positive predictive value of less than 50%. They conclude that using a blood eosinophil cutoff of 150 cells/ $\mu$ L would include many patients who do not have contemporaneous sputum eosinophilia and translate this into a potential lack of response or underestimation of response to new biologic medications, such as mepolizumab. For the mepolizumab program, the goal of using blood eosinophils as a biomarker is not to accurately predict the sputum eosinophil percentage but rather to serve as a marker of treatment response. Recently, we reported that sputum eosinophils do not predict treatment response to mepolizumab.<sup>2</sup> In contrast, blood eosinophils have been shown to predict treatment response in 2 large mepolizumab trials.<sup>3,4</sup>

As part of the Mepolizumab for Severe Eosinophilic Asthma (DREAM) study,<sup>3</sup> a substudy was conducted, collecting sputum and blood eosinophils. Among 76 patients with paired samples of sputum and blood eosinophils at screening, a blood eosinophil count of 150 cells/ $\mu$ L or greater correctly predicted sputum eosinophilia in 9 of 10 cases and demonstrated a sensitivity of 85% (95% CI, 73% to 93%) and specificity of 75% (95% CI, 48% to 93%). By using this threshold for blood eosinophils, there were only 4 patients with blood eosinophil counts of 150 cells/ $\mu$ L or greater and a sputum count of less than 2% and 9 patients who had a sputum count of 2% or greater and a blood eosinophil count of less than 150 cells/ $\mu$ L (Fig 1). Increasing the threshold to 300 cells/ $\mu$ L or greater, 1 patient had a sputum count of less than 2%, but 25 patients had a sputum count of 2% or greater, with a blood eosinophil count of less than 300 cells/ $\mu$ L. This threshold would have removed a significant number of patients with severe asthma who could benefit from mepolizumab. These data lend further support to the selection of 150 cells/ $\mu$ L or greater and

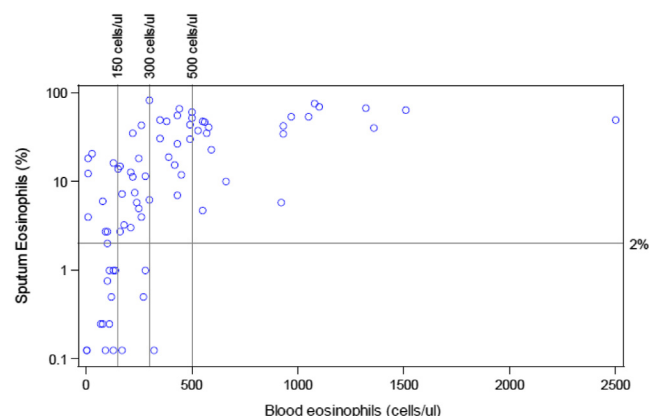


FIG 1. Display of sputum versus blood eosinophils at the screening visit.

demonstrate the utility for predicting airway eosinophilia and treatment response.

Similarly, a recent report in a population with severe asthma<sup>5</sup> identified the ideal cutoff as 188 cells/ $\mu$ L for blood eosinophils to detect sputum eosinophilia of 3% or greater with a sensitivity of 72% and specificity of 73%. These data are consistent with our results and support a cutoff of 150 cells/ $\mu$ L in a population with severe asthma. Differences in results across studies are expected when assessing different populations. Although the population reported in the letter by Fowler et al<sup>1</sup> is stated to have severe asthma, this population would not necessarily fully overlap with the population with severe asthma that is eligible for mepolizumab. Measuring eosinophilic inflammation is important in establishing a diagnosis, in monitoring and assessing response to treatment, and in testing novel therapeutics, such as biologics. A useful biomarker is one that represents the underlying pathologic mechanisms of disease and correlates with the mechanism of action of the biologic, allowing targeted therapy through personalized medicine. A biomarker should be minimally invasive, easily measured, and reproducible. Finally, personalized medicine should not be solely based on a biomarker but rather should be used in conjunction with careful characterization of the patient's clinical features.

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Disclosure of potential conflict of interest: H. Ortega, N. Gunsoy, O. Keene, and S. Yancey are employed by GlaxoSmithKline. L. Katz was employed by GlaxoSmithKline until April 2015. All of the authors have stock/stock options in GlaxoSmithKline.

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

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## Corrections

With regard to Abstract 375 published in the February 2015 issue entitled, “Elevated Serum Tryptase Levels during Rituximab Hypersensitivity Reaction” (*J Allergy Clin Immunol* 2015;135[suppl]:AB116), the authors would like make the following corrections: Patient 1 developed hypotension, hypoxia, and elevated tryptase on his second drug desensitization, not his third lifetime infusion. He was given intramuscular epinephrine and the infusion was aborted. Patient 2 developed hypotension, hypoxia, and elevated tryptase on her second desensitization, not second lifetime infusion. She was administered intramuscular epinephrine and completed the infusion. Both patients tolerated subsequent desensitizations. The authors regret these errors.

With regard to the article in the July 2015 issue entitled “Activated glycoprotein A repetitions predominant (GARP)–expressing regulatory T cells inhibit allergen-induced intestinal inflammation in humanized mice” (*J Allergy Clin Immunol* 2015;136:159-68), the authors report that the affiliation for 3 co-authors was listed incorrectly. The correct affiliation for Melanie Eschborn, Joachim Saloga, and Iris Bellinghausen is the Department of Dermatology, University Medical Center of the Johannes Gutenberg-University of Mainz, Mainz, Germany. The authors regret the error.