

of 63 months (range, 40.5-129 month). Patients were aged 55 years (range, 47.5-62 years) and 39.1% were women. Mean annual rate of asthma exacerbation was 1.74 ± 1.63 , median eosinophil count was $490/\text{mm}^3$ (range, 365-752), GC dose was 10 mg/d (range, 7.5-15 mg/d), and FEV₁ was 64% (range, 51% to 89%) (Figure 1). After 1 year of treatment, 62% of patients were responders, but only one was weaned from GCs (4.3%). We also observed significant improvement at 12 months in the rate of asthma exacerbation, median GC dose, blood eosinophil count, and FEV₁ (Figure 1). Treatment was switched to other IL5-blocking therapies in five patients: benralizumab (n = 3) or mepolizumab at 300 mg/4 wk (n = 2).

Our data confirm the findings of Caminati et al³ and suggest that mepolizumab 100 mg/4 wk may be effective as a GC-sparing agent in EGPA patients with persistent severe asthma after vasculitis remission. However, only one patient was GC-free at 12 months, whereas prednisone could be withdrawn in two additional patients after mepolizumab dose escalation to 300 mg/4 wk. This may suggest a dose-response effect. This lower rate of complete GC withdrawal is in accordance with the pivotal trial in which 18% of patients in the mepolizumab arm were able to discontinue GCs.³ These discrepancies may relate to differences in initial patients' characteristics or variations in concomitant asthma treatments.

Our study was limited by its retrospective design, the lack of a control group, and missing data. Nevertheless, these data confirm that mepolizumab 100 mg/4 wk may be effective in treating severe asthma in many EGPA patients with vasculitis in remission, but that a higher dose may be needed for optimal outcomes in some patients. A randomized trial would be highly interesting to confirm these findings.

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Reply to "Mepolizumab in patients with eosinophilic granulomatosis with polyangiitis in remission: What is the right dose?"



To the Editor:

We are grateful to Akdime and coauthors¹ for their valuable contribution to the debate on the place and relevance of anti-IL5 biologic treatments in eosinophilic granulomatosis with polyangiitis (EGPA), which currently represents a challenging hot topic. By confirming our data,² the study by Akdime and coauthors on mepolizumab 100 mg/4 wk in severely asthmatic patients with EGPA in the remission phase supports the concept that precisely defining a target population for a specific treatment and dose is essential when managing biologic drugs, especially in the context of EGPA. In fact, its pathogenesis is complex enough to offer different potential therapeutic targets, and identifying the most appropriate one is crucial to achieve disease control and attain the maximal steroid or immunosuppressive sparing effect of the selected treatment option.

As we pointed out in a recently published commentary³ on the real-life report about biologic drugs in EGPA by the European EGPA study group,⁴ in addition to demonstrating the general efficacy of biologics, validating a phenotype-tailored approach should be the goal. Indeed, the heterogeneity of the study population in terms of the type and entity of organ involvement when initiating mepolizumab treatment may be a potential explanation for the considerable proportion of patients who failed to reach the protocol-defined outcomes in the Mepolizumab In Relapsing or Refractory EGPA (MIRRA) trial.⁵

Although it is currently supported by limited evidence, the use of mepolizumab 100 mg/4 wk in patients with persisting severe asthma and EGPA in the remission phase relies on a strong rationale. From the pathophysiologic perspective, an EGPA march concept could be hypothesized. In fact, in patients experiencing severe asthma and EGPA, the two conditions can be considered different clinical expressions of the same underlying eosinophilic inflammation, in which EGPA represents the peak of its systemic manifestation and severe asthma is both a prodromal condition and a postvasculitis clinical stage.⁶ This background, together with strong evidence of the beneficial effects of mepolizumab 100 mg/4 wk in severe asthma,⁷ supports its use in a well-defined EGPA population, as described earlier.

In the study by Akdime and coauthors,¹ despite a documented steroid-sparing effect in the whole sample, only one patient withdrew from steroid treatment. In contrast, we reported that nine of 16 patients completely discontinued oral steroids (56.2%).² In our population, nine of 11 patients maintained the immunosuppressive drug 6 months after mepolizumab initiation, although four reduced the dose, and two completely stopped that treatment. Currently available recommendations do not indicate whether steroid rather than immunosuppressive agents should be withdrawn first in the maintenance phase. Because of the well-known effects of systemic steroid therapy on bones and metabolism, we decided to stop it first.

However, a number of open issues should be specifically addressed by further investigations, including the dose-response effect of biologics, their ability to prevent EGPA onset in severe asthmatic patients undergoing that treatment, and the

management of nonresponders. In this regard, we should not forget that eosinophilic inflammation targeted by anti-IL5 drugs represents only one mechanism underlying the complex picture of EGPA pathophysiology.

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Concerns about the approach of measuring allergens in early introduction foods for prevention of food allergy



To the Editor:

We would like to highlight the method limitations and assumptions in the article titled "Doses of specific allergens in early

introduction foods for prevention of food allergy"¹ as it relates to trying to measure certain proteins in early allergen foods (EIF).

Most notably, a methodology of extracting the proteins from various food matrices is best implemented with an approach that properly captures all proteins from those foods, not just some. Specifically, by not extracting on a per-serving basis, the quantifications do not accurately represent the proteins of each food product consumed. For example, methodology only allowed for analysis of fewer than 1 of 50 total puffs in a complete daily serving of SpoonfulONE. This evaluation is, therefore, hardly a representation of the food. Similarly, the authors did not standardize their measurements on a total-protein basis, further obfuscating the interproduct EIF comparisons. Moreover, the assumption of single-allergen measurement by antibodies to quantify the total protein does not account for all the proteins in a single ingredient, let alone multi-ingredient foods. Filep and Chapman's extrapolation of a food's protein content from unrepresentative, unequilibrated servings with select antibody coverage of proteins and their components is limited.

Our methods and formula were developed at the Sean N. Parker Center for Allergy and Asthma Research at Stanford University, and then transformed into a scalable and safe consumer product over the past 5 years using both independent commercial laboratory data and patent data from Stanford. We implement protein testing using SDS-PAGE and total protein by nitrogen content assays; with standards accepted by the U.S. Food and Drug Administration. It is a standard practice to ensure major protein components are preserved throughout the manufacturing process and in final products. Lastly, we check each product over the course of its shelf life (12 months) to ensure consistent protein integrity over time. All SpoonfulONE products are tested up to 3 times during manufacturing to ensure protein integrity of 16 food allergens (Figure 1). In our 3 years of production, we have run over 1,000 gels to obtain consistent and repeatable results for our products.

SpoonfulONE also tests all ingredients and products for microbiological (bacteria, fungi), chemical contaminants (heavy metals, toxins), and total protein. If an ingredient or product does not meet safety standards for infants, it is rejected. Our protein integrity and food safety analysis is performed by an independent, ISO 17025:2005 accredited laboratory—AEMTEK Laboratories. Representative samples from all lots of ingredients and SpoonfulONE products are tested, and cannot be released until all microbiological, chemical and SDS-PAGE analyses are complete and compliant.

In conclusion, we agree that scalable, reproducible protein integrity and quantification testing is needed in EIF; however, there are limitations in the methodology and extrapolations performed in the Filep and Chapman study.¹ Our products are tested with the highest standards for food safety and protein integrity, and we look forward to continuing to try to understand how early diet diversity in infants/toddlers may improve health.

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