Evaluation of clinical benefit from treatment with mepolizumab for patients with eosinophilic granulomatosis with polyangiitis

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Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss syndrome, is a rare multisystem disease characterized by asthma, sinusitis, blood and tissue eosinophilia, and systemic necrotizing vasculitis.1,2 The precise role of eosinophils in the pathology of EGPA remains unclear; however, evidence of blood eosinophilia; eosinophilic tissue infiltration of the lungs, heart, and gastrointestinal tract; and vascular and extravascular eosinophilic granulomatous inflammation, suggests that eosinophils are central to EGPA pathogenesis.1,3

Glucocorticoids reduce blood and tissue eosinophil counts by inducing apoptosis and inhibiting prosurvival signaling pathways.2 Based on long-term studies showing increased patient survival, oral glucocorticoids (OGCs) are currently recommended as first-line treatment for EGPA. However, relapses occur frequently, and many patients do not taper their OGC dose or discontinue OGC treatment.3,4,8,9 Chronic and high-dose OGC use is associated with serious and sometimes irreversible adverse effects, including increased risk of infection, osteoporosis, and secondary adrenal insufficiency.10,11 Even short courses of high-dose OGCs are associated with side effects.12 Immunosuppressive therapy is also recommended for remission-induction and as maintenance therapy in patients with EGPA.13 Although OGCs and immunosuppressive therapies are commonly used, they have not been systematically investigated in controlled trials for EGPA. Furthermore, expert opinion and small studies suggest that use of immunosuppressive agents does not substantially affect relapse rates.14 Considering the inadequate efficacy of OGCs in inducing relapse-free remission and the significant side effect burden associated with both OGCs and other immunosuppressive drugs, there is a pressing need for more effective and tolerable treatment options for EGPA.

Mepolizumab, an anti–IL-5 mAb that reduces blood and airway eosinophil counts,1,5 has been investigated as a potential therapy for patients with EGPA.15,16 A phase III trial was recently conducted to assess the efficacy and safety of mepolizumab in patients with relapsing and refractory EGPA over 52 weeks.5 The trial assessed 2 primary end points: total accrued weeks of remission (defined as Birmingham Vasculitis Activity Score [BVAS] of 0 and OGC dose of <4 mg/d) and the proportion of patients who experienced 24 or more weeks of accrued remission; 32% versus 3% of patients receiving mepolizumab versus 3% of patients receiving placebo experienced remission at weeks 36 and 48. Overall, 28% of patients receiving mepolizumab versus 3% of patients receiving placebo experienced 24 or more weeks of accrued remission; 32% versus 3%, respectively, had remission at both weeks 36 and 48. Although both primary end points were met, many patients in the mepolizumab treatment group did not achieve protocol-defined remission. However, it is further hypothesized that treatment with mepolizumab provided clinical benefits that were not encompassed by the trial’s predefined remission end points.

There are several aspects of clinical benefit aside from protocol-defined remission that are important to consider when assessing the efficacy of therapy in patients with EGPA. As such, determining the effect of mepolizumab treatment on clinical parameters additional to the primary and secondary end points of the phase III trial is of relevance to clinicians and patients with EGPA. The objective of this post hoc assessment was to gain a broader overview of the efficacy of mepolizumab in EGPA by investigating whether further clinical benefits in addition to those demonstrated in the original analysis were present. To do this, patient response was assessed by using a composite definition of clinical benefit that was based on the 3 objectives of treatment: remission, OGC dose reduction, and a reduction in the rate of relapse.

**METHODS**

**Study design and treatments**

The study design and treatment schedule of the phase III trial (GSK ID 1159211 and NCT02020889) have been reported previously.5 In brief, the study was a randomized, placebo-controlled, double-blind, parallel-group multicenter trial. After screening, which occurred 1 to 4 weeks before baseline, patients were randomly assigned (1:1) to receive 300 mg of subcutaneous mepolizumab (GlaxoSmithKline, Philadelphia, Pa) or placebo in addition to

**Abbreviations used**

BEC: Blood eosinophil count
BVAS: Birmingham Vasculitis Activity Score
EGPA: Eosinophilic granulomatosis with polyangiitis
EULAR: European League Against Rheumatism
OGC: Oral glucocorticoid
standard of care every 4 weeks for 52 weeks (final dose at week 48). This was followed by an 8-week follow-up period. Patients’ OGC doses had to remain stable from the initiation of screening (week –4) to week 4 but thereafter could be reduced by the investigator with a recommended tapering schedule.

**Patients**

To be enrolled in the study, patients had to be 18 years of age or older, have received a diagnosis of relapsing or refractory EGPA at least 6 months previously, and have received a stable dose of OGCs (prednisolone or prednisone, $\leq 7.5–\leq 50$ mg/d) with or without additional immunosuppressive therapy for 4 or more weeks before enrollment in the study. Further details of participant selection criteria are detailed in the primary publication. The trial was conducted in accordance with the Declaration of Helsinki, the International Conference on Harmonization Good Clinical Practice guidelines, and any applicable country-specific requirements. All participants provided written informed consent. The original study was approved by each local institutional review board.

**Post hoc assessments and end points**

Clinical benefit was a composite end point that was met if patients met at least 1 of the following 3 component end points, which were all pre-defined in the original study: (1) remission at any time during the study period (weeks 1–52), (2) a 50% or greater reduction in OGC dose during weeks 48 to 52, or (3) no relapses of EGPA during the study period (weeks 1–52). As in the original study, remission was defined by using 2 separate criteria: first, a BVAS of 0 plus an OGC dose of 4 mg/d or less (remission 1), and second, an alternative definition based on the European League Against Rheumatism (EULAR) recommendations for clinical studies in systemic vasculitis (BVAS of 0 plus an OGC dose $\leq 7.5$ mg/d [remission 2]). Therefore clinical benefit was defined as either clinical benefit 1 when encompassing the criteria for remission 1 or clinical benefit 2 when encompassing the criteria for remission 2. A relapse of EGPA was defined as active vasculitis (BVAS $>0$), active asthma symptoms with a corresponding worsening score on the Asthma Control Questionnaire-6, or worsening sinonasal symptoms requiring an increase in OGC dose to greater than 4 mg/d, an initiation or increase of immunosuppressive therapy, or hospitalization.

Descriptive statistics were used to summarize the proportion (numbers and percentages of total) of patients to meet each definition of clinical benefit. Analyses were performed by using the as-treated population. Statistical analyses of treatment response for mepolizumab versus placebo were performed by using a 2-sided Fisher exact test.

**Subgroups of clinical interest**

End points were also assessed in specific subgroups of clinical interest, including baseline blood eosinophil counts (BECs) of less than 150 cells/$\mu$L, and baseline OGC doses of greater than 20 mg/d. Response to mepolizumab in terms of accrued duration of remission has been reported to be lower in these patient populations than in the general EGPA population. The subgroup of patients weighing more than 85 kg was also investigated because weight is the only characteristic that has been associated with pharmacokinetic exposure for this biologic.

**RESULTS**

**Patient population**

Of the 151 patients enrolled in the phase III study, 136 underwent randomization; 68 were randomly assigned to receive mepolizumab, and 68 were randomly assigned to receive placebo. All patients were included in the current analysis. Because one patient randomized to placebo received mepolizumab and another patient randomized to mepolizumab received placebo, analyses were carried out with as-treated treatment group allocations rather than randomized treatment assignments. Demographic and baseline clinical characteristics of the patients are summarized in Table I.

**Efficacy within the as-treated population**

**Composite end point.** By using the composite end point, the proportion of patients experiencing any clinical benefit after treatment with mepolizumab ranged from 78% to 87% depending on the remission criteria used (Fig 1) compared with 32% to 53% of patients receiving placebo.

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**TABLE I. Summary of patients’ demographic characteristics and diagnostic and baseline characteristics of EGPA (as-treated population)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n = 136)</th>
<th>BEC &lt;150 cells/$\mu$L (n = 57)</th>
<th>BEC $\geq$150 cells/$\mu$L (n = 79)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (y), mean (SD)</strong></td>
<td>48.5 (13.3)</td>
<td>50.4 (12.8)</td>
<td>47.1 (13.6)</td>
</tr>
<tr>
<td><strong>Male sex, no. (%)</strong></td>
<td>56 (41)</td>
<td>28 (49)</td>
<td>28 (35)</td>
</tr>
<tr>
<td><strong>ANCA-positive status, no. (%)</strong>*</td>
<td>13 (10)</td>
<td>5 (9)</td>
<td>8 (10)</td>
</tr>
<tr>
<td><strong>BVAS $&gt;0$, no. (%)†</strong></td>
<td>85 (63)</td>
<td>35 (61)</td>
<td>50 (63)</td>
</tr>
<tr>
<td><strong>Immunosuppressive therapy at baseline, no. (%)</strong></td>
<td>72 (53)</td>
<td>34 (60)</td>
<td>38 (48)</td>
</tr>
<tr>
<td><strong>Presence of EGPA disease characteristics at any time during disease course, no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asthma with eosinophilia</strong></td>
<td>136 (100)</td>
<td>57 (100)</td>
<td>79 (100)</td>
</tr>
<tr>
<td><strong>Biopsy evidence‡</strong></td>
<td>56 (41)</td>
<td>22 (39)</td>
<td>34 (43)</td>
</tr>
<tr>
<td><strong>Neuropathy§</strong></td>
<td>56 (41)</td>
<td>23 (40)</td>
<td>33 (42)</td>
</tr>
<tr>
<td><strong>Nonfixed pulmonary infiltrates</strong>§</td>
<td>98 (72)</td>
<td>43 (75)</td>
<td>55 (70)</td>
</tr>
<tr>
<td><strong>Sinonasal abnormality</strong></td>
<td>128 (94)</td>
<td>55 (96)</td>
<td>73 (92)</td>
</tr>
<tr>
<td><strong>Cardiomyopathy</strong>†</td>
<td>20 (15)</td>
<td>9 (16)</td>
<td>11 (14)</td>
</tr>
<tr>
<td><strong>Glomerulonephritis</strong></td>
<td>1 (&lt;1)</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Alveolar hemorrhage</strong></td>
<td>4 (3)</td>
<td>1 (2)</td>
<td>3 (4)</td>
</tr>
<tr>
<td><strong>Pulmonary edema</strong></td>
<td>17 (13)</td>
<td>4 (7)</td>
<td>13 (16)</td>
</tr>
<tr>
<td><strong>Anemia</strong></td>
<td>26 (19)</td>
<td>12 (21)</td>
<td>14 (18)</td>
</tr>
<tr>
<td><strong>Relapsing disease, no. (%)</strong></td>
<td>100 (74)</td>
<td>45 (79)</td>
<td>55 (70)</td>
</tr>
<tr>
<td><strong>Refractory disease, no. (%)</strong></td>
<td>74 (54)</td>
<td>28 (49)</td>
<td>46 (58)</td>
</tr>
<tr>
<td><strong>Duration since diagnosis of EGPA (y), mean (SD)</strong></td>
<td>5.5 (4.6)</td>
<td>6.1 (5.0)</td>
<td>5.2 (4.3)</td>
</tr>
<tr>
<td><strong>Immunosuppressive therapy since diagnosis, no. (%)</strong></td>
<td>105 (77)</td>
<td>45 (79)</td>
<td>70 (66)</td>
</tr>
<tr>
<td><strong>Baseline OGC dose (mg/d), no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq$7.5</td>
<td>18 (13)</td>
<td>5 (9)</td>
<td>13 (16)</td>
</tr>
<tr>
<td>$&gt;$7.5 to $\leq$12</td>
<td>55 (40)</td>
<td>16 (28)</td>
<td>39 (49)</td>
</tr>
<tr>
<td>$&gt;$12 to $\leq$20</td>
<td>42 (31)</td>
<td>21 (37)</td>
<td>21 (27)</td>
</tr>
<tr>
<td>$&gt;$20</td>
<td>21 (15)</td>
<td>15 (26)</td>
<td>6 (8)</td>
</tr>
</tbody>
</table>

ANCA, Antineutrophil cytoplasmic antibody.

†Positive ANCA status for myeloperoxidase or proteinase 3 was assessed at screening by means of immunoassay performed at the Covance Laboratories (Princeton, NJ) and Q Solutions (Morrisville, NC).

‡The BVAS was assessed on a scale of 0 to 63, with higher scores indicating greater disease activity.

§Biopsy evidence was defined as a biopsy specimen showing histopathologic evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation.

|$<1$ | 1 (<1) | 1 (2) | 3 (4) |
|Palpable purpura| 17 (13)| 4 (7) | 13 (16)|
|ANCA positive| 26 (19)| 12 (21)| 14 (18)|
|Relapsing disease, no. (%)| 100 (74)| 45 (79)| 55 (70)|
|Refractory disease, no. (%)| 74 (54)| 28 (49)| 46 (58)|
|Duration since diagnosis of EGPA (y), mean (SD)| 5.5 (4.6)| 6.1 (5.0)| 5.2 (4.3)|
|Immunosuppressive therapy since diagnosis, no. (%)| 105 (77)| 45 (79)| 70 (66)|
|Baseline OGC dose (mg/d), no. (%)| | | |
|$\leq$7.5| 18 (13)| 5 (9)| 13 (16)|
|$>$7.5 to $\leq$12| 55 (40)| 16 (28)| 39 (49)|
|$>$12 to $\leq$20| 42 (31)| 21 (37)| 21 (27)|
|$>$20| 21 (15)| 15 (26)| 6 (8)|

ANCA, Antineutrophil cytoplasmic antibody.

*Positive ANCA status for myeloperoxidase or proteinase 3 was assessed at screening by means of immunoassay performed at the Covance Laboratories (Princeton, NJ) and Q Solutions (Morrisville, NC).

†The BVAS was assessed on a scale of 0 to 63, with higher scores indicating greater disease activity.

‡Biopsy evidence was defined as a biopsy specimen showing histopathologic evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation.

§Neuropathy was defined as a mononeuropathy or polyneuropathy (motor deficit or nerve-conduction abnormality).
When remission was defined as a BVAS of 0 plus an OGC dose of 4 mg/d or less (remission 1) at any time during the study period, 78% (53/68) of patients in the mepolizumab group compared with 32% (22/68) in the placebo group experienced clinical benefit 1 (P < .001; Fig 1, A).

When the definition of clinical benefit included the EULAR remission criteria of a BVAS of 0 plus an OGC dose of 7.5 mg/d or less (remission 2), the proportion of patients experiencing clinical benefit 2 was 87% (59/68) in the mepolizumab group versus 53% (36/68) in the placebo group (P < .001; Fig 1, B). This increase in the proportion of patients experiencing clinical benefit was driven by an increase to 79% (54/68) of patients in the mepolizumab group and 46% (31/68) of patients in the placebo group achieving EULAR-defined remission during the study period.

**Individual components of the composite end point.** When assessing the individual components from the composite end point, 53% (36/68) of patients receiving mepolizumab achieved remission 1 (BVAS = 0 plus OGC dose ≤ 4 mg/d) at any time during the study period compared with 19% (13/68) of patients receiving placebo (P < .001). Additionally, 57% (39/68) of patients receiving mepolizumab were able to reduce their OGC dose by 50% or greater compared with 21% (14/68) of patients receiving placebo (P < .001), and 44% (30/68) of patients receiving mepolizumab were relapse free versus 18% (12/68) of patients receiving placebo (P = .001; Fig 1, A).

**Combinations of components included in the composite end point.** In addition to assessing the proportion of patients who met the composite end point, a more detailed analysis was conducted of the proportion of patients who met each combination of component end points (Fig 2). Overall, 29% (20/68) of patients in the mepolizumab group met all 3 definitions of clinical benefit 1 (remission 1 at any time [BVAS = 0 plus OGC dose ≤ 4 mg/d] plus ≥ 50% OGC dose reduction and no EGPA relapses) compared with only 7% (5/68) of patients in the placebo group (Fig 2). Notably, 25% (17/68) of patients receiving mepolizumab versus 13% (9/68) of patients receiving placebo achieved a 50% or greater reduction in OGC dose, no EGPA relapses, or both, despite not achieving remission 1 (BVAS = 0 plus OGC dose ≤ 4 mg/d). Fifteen (22%) patients receiving mepolizumab were unable to meet any of the 3 components of clinical benefit compared with 46 (68%) of the patients receiving placebo (Fig 2).

**Efficacy within selected clinical subgroups**

**Baseline BEC.** For patients with baseline BECs of less than 150 cells/μL, there was evidence of clinical benefit from treatment with mepolizumab. When clinical benefit included remission 1 (BVAS = 0 plus OGC ≤ 4 mg/d), patients in this subgroup receiving mepolizumab experienced significantly greater clinical benefit than patients receiving placebo; overall, 72% (21/29) of patients receiving mepolizumab experienced clinical benefit 1 compared with 43% (12/28) of patients receiving placebo (P = .033; Fig 3, A). When clinical benefit included remission 2 (BVAS = 0 plus OGC dose ≤ 7.5 mg/d), the increase in clinical benefit observed among patients receiving mepolizumab versus patients receiving placebo was not significant at the 5% level but was directionally in favor of mepolizumab; 79% (23/29) of patients receiving mepolizumab experienced clinical benefit 2 compared with 54% (15/28) of patients receiving placebo (P = .052; Fig 3, A).

**OGC dose.** For patients with baseline OGC doses of greater than 20 mg/d, treatment with mepolizumab did not lead to a
significant increase in clinical benefit compared with treatment with placebo; however, results were directionally in favor of mepolizumab compared with placebo. When clinical benefit included remission 1 (BVAS = 0 plus OGC dose ≤4 mg/d), 60% (6/10) of patients in the mepolizumab treatment group experienced clinical benefit 1 compared with 36% (4/11) of patients in the placebo group (P = .359; Fig 3, B). When clinical benefit included remission 2, 70% (7/10) of patients in the mepolizumab treatment group compared with 36% (4/11) of patients in the placebo group experienced clinical benefit 2 (P = .198; Fig 3, B).

**Baseline weight.** Within the subgroup of patients with baseline weight of greater than 85 kg, mepolizumab provided greater clinical benefit than placebo for both definitions of clinical benefit. When clinical benefit included the remission definition of a BVAS of 0 plus OGC dose ≤4 mg/d or less (remission 1), 68% (13/19) of patients receiving mepolizumab experienced clinical benefit 1 compared with 23% (6/26) of patients receiving placebo (P = .005; Fig 3, C). When clinical benefit included the EULAR remission criteria (remission 2), 89% (17/19) of patients receiving mepolizumab experienced clinical benefit 2 compared with 46% (12/26) of patients receiving placebo (P = .004; Fig 3, C).

**DISCUSSION**

These post hoc analyses provide a broader overview of the efficacy of mepolizumab in patients with relapsing or refractory EGPA by using data from the recent phase III trial. The primary end point in the phase III clinical trial, total accrued time of remission, was developed with the US Food and Drug Administration for regulatory purposes and was designed to capture a meaningful difference because of treatment in a condition with frequent relapses. What is notable here is that patients also experienced additional forms of clinical benefit that had a substantial influence on their experience of disease, such as a lack of EGPA relapse or a reduction in OGC dose. By using a broader but still clinically relevant definition of clinical benefit, these assessments provide additional insight into patient responses to treatment with mepolizumab.

There are many reasons why a patient might have been able to meet one definition of clinical benefit but not another, depending on the specific nature of their disease. In particular, an OGC dose of 4 mg/d or less (required to meet protocol-defined remission) would have been difficult to achieve for patients with a high burden of disease who entered the study on a dose of greater than 20 mg/d. However, results from the current assessments show that patients who did not achieve remission might have experienced other forms of clinical benefit, such as having a 50% or greater decrease in daily OGC dose compared with baseline and being relapse free (exacerbation free) throughout the study period.

There was a relatively high response rate in the placebo group (up to 53%) when using the definition of clinical benefit that used either remission criteria. This might indicate that many patients were receiving greater OGC doses than necessary at baseline and highlights the importance of optimizing patients’ OGC doses in clinical practice.

Overall, among patients with baseline BECs of less than 150 cells/μL, a greater proportion of patients experienced clinical benefit with mepolizumab versus placebo. In this subgroup higher proportions of patients receiving mepolizumab achieved a 50% or greater reduction in OGC dose during weeks 48 to 52 and were relapse free during the treatment period compared with patients receiving placebo. For clinical benefit 1 (remission criteria 1: BVAS = 0 and OGC ≤4 mg/d) but not clinical benefit 2 (remission criteria 2: BVAS = 0 and OGC ≤7.5 mg/d), a significantly greater proportion of patients receiving mepolizumab experienced any clinical benefit compared with patients receiving placebo. Of note, patients with BECs of less than 150 cells/μL more
Remission 1 criteria: BVAS of 0 plus OGC dose of 4 mg/d or less; remission 2 criteria: BVAS of 0 plus OGC dose of 7.5 mg/d or less.

Figure 3. Summary of clinical benefit in the baseline BEC of less than 150 cells/µL (A) n = 57, baseline OGC dose of greater than 20 mg/d (B) n = 21, and weight of greater than 85 kg (C) n = 45 subgroups. Clinical benefit was defined as follows: clinical benefit 1 (remission 1 at any time during the study treatment period or ≥50% reduction in average OGC dose during weeks 48–52 or no EGPA relapses during the study period) or clinical benefit 2 (remission 2 at any time during the study treatment period or ≥50% reduction in average OGC dose during weeks 48–52 or no EGPA relapses during the study period). Remission 1 criteria: BVAS of 0 plus OGC dose of 4 mg/d or less; remission 2 criteria: BVAS of 0 plus OGC dose of 7.5 mg/d or less.
commonly had a greater baseline OGC dose, making it harder for them to achieve protocol-defined remission while following the recommended tapering schedule. This might partially explain why mepolizumab has previously been associated with a lower accrued duration of remission in patients with a BEC of less than 150 cells/μL compared with patients with a BEC of 150 cells/μL or greater.\(^5\)^ In the subgroup of patients with a baseline OGC dose of greater than 20 mg/d, results for the individual components of the composite end point were not consistent; however, the proportions of patients to experience any clinical benefit \(^1\) and clinical benefit \(^2\) were greater among patients treated with mepolizumab versus those treated with placebo (not significant). Additionally, in the subgroup of patients with weights of greater than 85 kg, significantly greater proportions of patients treated with mepolizumab versus patients treated with placebo experienced clinical benefit \(^1\) and clinical benefit \(^2\).

Other studies that have investigated the use of mepolizumab for the treatment of EGPA have also reported on the ability of mepolizumab to induce remission, prevent relapses, and allow a reduction in glucocorticoid dose.\(^13\)^ In a pilot study of mepolizumab in patients with EGPA,\(^15\) the glucocorticoid-sparing effect of mepolizumab was investigated as a primary end point. A 64% reduction in mean OGC dose, from 12.9 mg/d at baseline to 4.6 mg/d after 12 weeks of therapy \((P < .001)\), was observed. Additionally, in a phase II trial of mepolizumab,\(^16\) 80% (8/10) of patients achieved remission (EULAR remission criteria) at week 32, 100% (10/10) of patients experienced no EGPA relapses during treatment, and the median daily glucocorticoid dose was reduced from 19 mg at baseline to 4 mg at week 32 \((P = .006)\). The glucocorticoid-sparing effect of mepolizumab is also supported by the results of the recent phase III trial.\(^5\) During weeks 48 to 52, 44% (30/68) of patients receiving mepolizumab versus 7% (5/68) of patients receiving placebo were able to taper their OGC dose to 4 mg/d or less, and 18% (12/68) versus 3% (2/68), respectively, were able to discontinue OGC completely.\(^5\) These results support the concept that clinical response to mepolizumab in patients with EGPA extends beyond remission and encompasses other benefits, including a decrease in daily OGC dose, with the potential for a reduction in dose-related side effects. Further work is currently underway to identify biomarkers that can predict disease activity or relapse in patients with EGPA and might help to identify those who could be more responsive to treatment.

This analysis had several limitations. First, the number of patients in the baseline OGC dose of greater than 20 mg/d subgroup was low \((n = 21)\), and therefore caution should be taken when interpreting the results for this particular subgroup. Second, because of the ability of OGCs to suppress BECs, patients with greater baseline OGC doses would have been more likely to have lower baseline BECs. As such, there was considerable correlation between the baseline OGC dose of greater than 20 mg/d and baseline eosinophil count of less than 150 cells/μL subgroups.

This assessment of the recent mepolizumab phase III clinical trial\(^5\) investigated a broader definition of clinical benefit to help classify and assess treatment response in patients with relapsing or refractory EGPA. The results presented here show that treatment with mepolizumab provides clinical benefit by allowing a reduction in OGC dose in most patients. Additionally, patients experienced clinical benefit through a decrease in the number of EGPA relapses, which, even in the absence of remission, means that patients are subject to fewer increases in glucocorticoid dose to manage their disease. Overall, the analyses performed in this study provide insights that are complementary to those of the phase III primary end point assessment and identify clinical responses to mepolizumab that are meaningful to both patients and providers.

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**Clinical implications:** Mepolizumab provides clinical benefit in terms of remission, glucocorticoid dose reduction, and reduced relapses in patients with relapsing or refractory EGPA.

**REFERENCES**


