

Mepolizumab as a steroid-sparing treatment option in patients with Churg-Strauss syndrome

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Background: Treatments for Churg-Strauss syndrome (CSS), a rare eosinophilic vasculitis characterized by asthma, sinusitis, peripheral eosinophilia, pulmonary infiltrates, and tissue infiltration, are limited by toxicity or poor efficacy. Levels of IL-5, a cytokine regulating eosinophils, can be increased in patients with CSS. Mepolizumab, a humanized monoclonal anti-IL-5 antibody, decreases steroid requirements in patients with non-CSS hypereosinophilic syndromes.

Objective: The purpose of this study was to assess whether mepolizumab would safely allow corticosteroid tapering in patients with steroid-dependent CSS while decreasing serum markers of disease activity.

Methods: This open-label pilot study treated 7 patients with 4 monthly doses of mepolizumab to assess whether it safely decreased CSS disease activity and permitted tapering of systemic corticosteroids.

Results: Mepolizumab was safe and well tolerated in patients with CSS. Mepolizumab reduced eosinophil counts and allowed for safe corticosteroid reduction in all 7 subjects. On cessation of mepolizumab, CSS manifestations recurred, necessitating corticosteroid bursts.

Conclusion: Mepolizumab is a safe and well-tolerated therapy in patients with CSS, offering clinical benefit by enabling corticosteroid tapering while maintaining clinical stability. (J Allergy Clin Immunol 2010;125:1336-43.)

Key words: Churg-Strauss syndrome, eosinophilia, IL-5, asthma, mepolizumab, steroid sparing

Abbreviations used

ACQ: Asthma Control Questionnaire
BVAS: Birmingham Vasculitis Activity Score
CRP: C-reactive protein
CSS: Churg-Strauss syndrome
ESR: Erythrocyte sedimentation rate
FeNO: Fraction of exhaled nitric oxide

Churg-Strauss syndrome (CSS; allergic granulomatosis and angiitis) is a hypereosinophilic syndrome characterized by small-vessel vasculitis and peripheral eosinophilia in association with asthma, sinusitis, and pulmonary infiltrates. CSS can affect the nerves, heart, skin, kidneys, and gastrointestinal tract. Amongst asthmatics, this rare syndrome has an incidence of approximately 35 to 64 cases per million person-years.^{1,2} Treatments are limited to systemic corticosteroids and immunomodulators, such as cyclophosphamide and azathioprine, all of which have significant side effects and might be ineffective.

The mechanism of tissue injury is poorly understood, but the degree of blood and tissue eosinophilia appears to be associated with disease pathogenesis.³ IL-5 mediates eosinophil bone marrow release, tissue survival, maturation, and activation. IL-5 levels are increased in patients with CSS and might correlate with disease activity.⁴ Thus neutralization of IL-5 with associated reduction in eosinophil numbers and activation provides a rational approach for the management of CSS. Indeed, a recent case report demonstrated efficacy of anti-IL-5 in a patient with CSS.⁵

Preliminary studies with 2 anti-IL-5 antibodies, SCH55700 (Schering-Plough, Deerfield, Ill) and mepolizumab (GlaxoSmithKline, Research Triangle Park, NC), demonstrated dramatic and prolonged reduction of peripheral eosinophil counts in patients with different hypereosinophilic syndromes, regardless of baseline IL-5.⁶⁻⁸ Furthermore, Rothenberg et al⁹ demonstrated that mepolizumab was well tolerated and significantly reduced steroid dosing, with maintenance of clinical stability in non-CSS FIP1L1-PDGFR α -negative hypereosinophilic syndrome. Although some studies of anti-IL-5 in patients with asthma have demonstrated a significant reduction in blood and sputum eosinophil counts^{10,11} independent of FEV₁ or symptom scores, recent trials of mepolizumab in patients with eosinophilic asthma significantly reduced asthma exacerbations.^{12,13}

We hypothesized that adjunct therapy with mepolizumab would safely allow corticosteroid tapering in patients with

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TABLE I. American College of Rheumatology CSS classification criteria¹⁴

This definition includes the presence of at least 4 of the following:

- Eosinophil count >10% of peripheral blood leukocytes on more than one occasion off prednisone therapy (historical)
- Asthma
- Neuropathy (mono or poly)
- Pulmonary infiltrates
- Paranasal sinus abnormality
- Extravascular eosinophils

steroid-dependent CSS while decreasing serum markers of disease activity.

METHODS

This open-label pilot study was approved by the Brigham and Women's Hospital Institutional Review Board. Patients were recruited nationally through the clinicaltrials.gov Web site and the investigators' clinical practices.

Inclusion/exclusion criteria

Inclusion criteria included a diagnosis of CSS as defined by the American College of Rheumatology classification criteria (Table I)¹⁴ and a requirement to be maintained on a stable dose of at least 10 mg of prednisone daily (or equivalent) before enrollment. Subjects receiving adjunct therapies, such as cyclophosphamide, azathioprine, or methotrexate, were required to maintain a stable dose so that medication withdrawal would not obfuscate potential drug benefits.

Subjects were excluded for non-CSS hypereosinophilic syndromes, Wegener granulomatosis, malignancy, or parasitic disease. Pregnant or nursing female patients were excluded because of the unknown drug safety profile. Female subjects with child-bearing potential were required to have a negative pregnancy test result and adhere to acceptable methods of contraception.

Study schema

The study was divided into 4 phases (Fig 1). During the initial screening phase, subjects provided informed consent, medical history was reviewed, and a physical examination was performed. Study physicians confirmed CSS diagnosis by means of history and medical record review. The lowest possible steroid dose was established based on medical record reviews with historical documentation that an attempted taper failed, evidence of clinical exacerbation below the presenting baseline dose, or both.

The treatment phase consisted of 4 monthly visits, at each of which subjects received 750 mg of mepolizumab infusions intravenously in the Infusion Center at Brigham and Women's Hospital. Phlebotomy for serum/blood markers of disease activity, spirometry, and measurement of fraction of exhaled nitric oxide (FeNO) were performed and questionnaires were administered at each visit. Patients were monitored for 1 hour after each 30-minute infusion.

Corticosteroid dose tapering began 2 weeks after the initial infusion and continued every 2 weeks according to a schedule based on the investigator's clinical experience (see Appendix 1). The washout phase consisted of physicians' monitoring subject stability as steroid doses were reduced and mepolizumab concentrations were decreased. Physicians monitored stability either with a study visit or by means of telephone contact. Telephone contact tapers were considered in concert with peak flow measurements, Asthma Control Questionnaire (ACQ) evaluation, and history. The final steroid dose was established 4 weeks after the final infusion. The safety-monitoring phase was used to assess patient stability on a stable tapered dose. Subjects were scheduled for 4 visits every 4 to 6 weeks. Serum markers and spirometric results were obtained, and questionnaires were administered as described above.

Outcomes

The primary objective was to assess whether mepolizumab safely decreased CSS disease activity and permitted scheduled tapering of systemic corticosteroids. In addition to assessment of treatment-related adverse effects, the primary outcome was the lowest prednisone dose achieved at the end of the treatment phase. Baseline and intrastudy disease activity were monitored by using blood and serum markers of disease (complete blood count with differential, erythrocyte sedimentation rate [ESR], antineutrophil cytoplasmic antibody, C-reactive protein [CRP], and IgE). Asthma activity was assessed by means of spirometry and the ACQ.¹⁵ Systemic vasculitic activity was assessed by using the Birmingham Vasculitis Activity Score (BVAS).¹⁶ FeNO was measured to evaluate underlying airway inflammation. Exacerbations were characterized as any worsening of clinical disease requiring escalation of systemic corticosteroid therapy for asthma, respiratory symptoms, or underlying vasculitis. Patients' ability to taper at each step was evaluated by study physicians based on peak flow measurements and clinical history.

RESULTS

Five female and 2 male patients enrolled and completed the study (mean age, 45 years; range, 28-62 years). All met American College of Rheumatology clinical criteria, and all had historical eosinophil counts of greater than 10%. All of the patients identified themselves as white. Two were undergoing methotrexate therapy, and one was receiving both methotrexate and hydroxychloroquine before enrollment. These 3 patients remained on stable doses of these therapies throughout the study. At baseline, mean FEV₁ was 76% of predicted value, and mean eosinophil count was 3.4% with a mean prednisone dose of 12.9 mg. BVAS (6.9), CRP (3.9 mg/L), and ESR (7 mm/h) indicated disease stability at baseline.

Mepolizumab was well tolerated, and there were no severe adverse events. Three patients noted mild transient headaches within 48 hours of infusion that resolved on their own or with 1 dose of over-the-counter analgesics. One patient noted mild pruritus for 1 to 2 days after infusion. There was no urticaria, evidence of allergic reaction, or worsening of symptoms with subsequent infusions, and symptoms resolved without intervention. There was 1 complaint of loose stools 1 day after infusion that self-resolved within 24 hours. Subjects experienced wheeze or cough (n = 4), sore throat (n = 4), nausea or abdominal discomfort (n = 3), sinusitis (n = 6), and arthritis (n = 1) during the trial. These symptoms occurred at least 6 days after the infusions and were not believed to be directly related to mepolizumab administration. Rather, they were presumably related to corticosteroid tapering, signs of CSS activity, or both.

Mepolizumab effectively served as a corticosteroid-sparing therapy. The mean dose at baseline was 12.9 mg/d (range, 10-20 mg). The mean dose after 12 weeks of therapy (study week 16) was 4.6 mg, a 64% reduction ($P = .0001$) after 4 doses of mepolizumab. The mean corticosteroid dose at the end of the washout phase (study week 24) was 5 mg, a 61% decrease ($P = .02$). At the completion of the study (week 40), the mean prednisone dose was 15.7 mg.

Subjects remained clinically stable during the treatment phase and variably so during the washout phase, with a concomitant decrease in percentage of eosinophils despite the steroid taper. However, on cessation of mepolizumab, CSS manifestations recurred, necessitating steroid bursts with a more gradual resurgence of percentage eosinophils as patients got further out from therapy (Fig 2). There were 20 CSS-associated exacerbations. Some patients had multiple exacerbations, and only

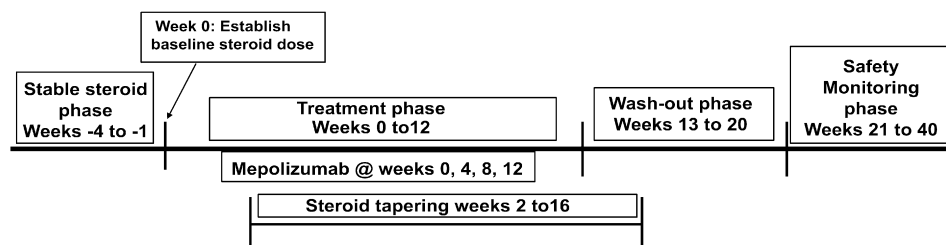


FIG 1. Study design. After a 3-week period during which a stable dose of corticosteroids was established (the stable steroid phase), subjects began treatment with 4 monthly doses of mepolizumab. Two weeks after the first dose, subjects began to taper corticosteroids based on a predetermined schedule. After the fourth dose, subjects were monitored during a 6-week washout phase followed by a 16-week safety-monitoring phase.

1 patient had none. Two occurred during the treatment phase, which was equivalent to a rate of 0.14 events per week; these consisted of worsening asthma. During the washout phase, there were 4 exacerbations (0.67 per week), and during the final safety-monitoring phase, there were 14 exacerbations (0.7 per week). Thus the exacerbation rate during the treatment period was 0.14 (2 events during a 14-week period), and the rate during the nontreatment period was 0.69 (18 events over a 26-week period). Based on this, we calculated *P* values by applying generalized estimating equations with a Poisson regression model to compare the significant exacerbation rates among the 3 periods. The difference between the treatment period versus the posttreatment period (A vs B+C) was significant (*P* = .017). The most common clinical complaints defining an exacerbation were wheezing and shortness of breath, cough, nausea, abdominal pain, sinusitis, diarrhea, and arthritis. Some patients were also noted to have decreased FEV₁, increased FeNO, or an increase in the ACQ score associated with the exacerbation. Exacerbations were treated with steroid bursts, ranging from 20 to 60 mg of prednisone, with a wide range of tapering schedules depending on severity. ACQ scores improved initially with mepolizumab therapy, decreasing from 1.57 at baseline to 0.71 during the treatment phase (*P* = .055). They subsequently worsened to 1.65 during the safety-monitoring phase. Although patients were able to reduce corticosteroid doses with mepolizumab treatment, other clinical markers of CSS activity (FEV₁, peak expiratory flow, FeNO, BVAS, CRP, and ESR) did not change significantly with therapy, nor did they worsen during the washout phase (Table II).

DISCUSSION

CSS remains a challenge for clinicians because the current standard-of-care therapies, corticosteroids and immunomodulators, do not always control symptoms and are often associated with significant morbidity. New therapies are urgently needed. However, because this is a rare orphan disease, testing novel therapies is challenging because few centers have sufficient numbers of patients to undertake randomized placebo-controlled trials.

Based on this pilot trial, it appears that adjuvant therapy with mepolizumab might allow for substantial corticosteroid tapering while maintaining clinical stability. There was a decrease in mean steroid dose from 12.9 to 4.6 mg/d after 12 weeks of therapy. Given the substantial side effect burden that patients undergoing chronic steroid therapy bear, including weight gain, thinning skin,

increased risk of infection, adrenal suppression, osteoporosis, cataracts, glaucoma, hyperglycemia, and depression, we believed that this decrease was a significant clinical benefit. Eosinophilia decreased considerably but returned to pretreatment levels after mepolizumab was withdrawn. Similarly, the pattern of exacerbations and clinical symptoms appeared to improve while patients were receiving therapy and then worsened after withdrawal. The treatment phase had the fewest exacerbations and was found to be significantly lower than the number of incidents during the washout and safety-monitoring (nontreatment) phases. Mean steroid dose was appreciably higher during these phases because of the quantity and duration of steroid bursts required to control symptoms. Although there were some individual variations among patients in regard to the timing and frequency of exacerbations, one must keep in the mind the wide clinical variability present in any syndrome. Overall, the general trend in this pilot study appeared to support the primary outcome. The difference in ACQ scores approached statistical significance but did not reach it. Given the small sample size of this pilot study, we believe that this at least suggests that mepolizumab has some efficacy in attenuating symptoms.

CSS activity was monitored based on several objective criteria, although it is recognized that no standardized validated tool for the assessment of disease activity in patients with CSS currently exists. Similarly, treatment of CSS exacerbations is not standardized. As such, the steroid bursts and subsequent titration used to treat exacerbations was at the discretion of the clinician. We attempted to burst patients in a manner that was commensurate with their exacerbation, with the hope of maximizing patient safety and mimicking real-world conditions. Future studies will use a standardized titration method to keep the steroid dose at the minimum necessary to address the exacerbation. Although there was no improvement in other markers of disease activity, there was no decrement, as might be expected in patients who are treated with lower steroid doses. Although it is possible that the baseline corticosteroid dose was higher than what was needed to control the disease, all of the patients enrolled in the study had previously failed multiple tapers below their baseline dose, suggesting that the mepolizumab did indeed result in disease control in these patients. This became more apparent during the washout phase, when subjects had worsening disease control as mepolizumab levels presumably decreased. This study's findings also emphasize the association between eosinophilia and CSS disease activity. However, the lack of improvement in pulmonary function despite reduced eosinophil counts suggests that other variables contribute to CSS airway disease. Further studies are

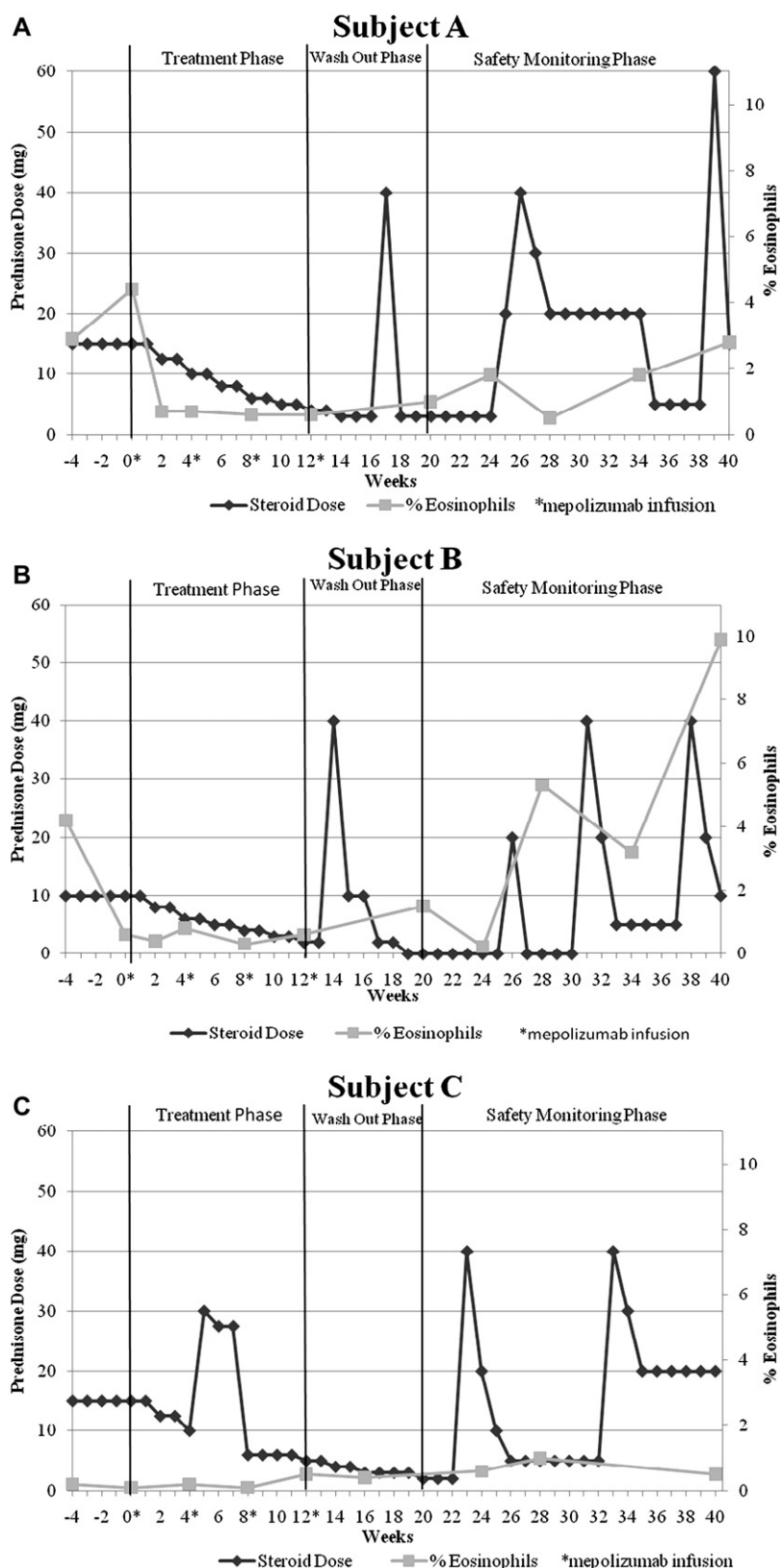


FIG 2. These graphs compare steroid doses and percentages of eosinophils for each subject over the course of the study. Eosinophil levels appear to decrease during the treatment and washout phases despite the steroid tapering. Eosinophils levels subsequently increase during the latter part of the washout and safety-monitoring phases, presumably as mepolizumab levels waned. In most cases the frequency of steroid bursts in response to clinical exacerbations increased with increasing eosinophil levels.

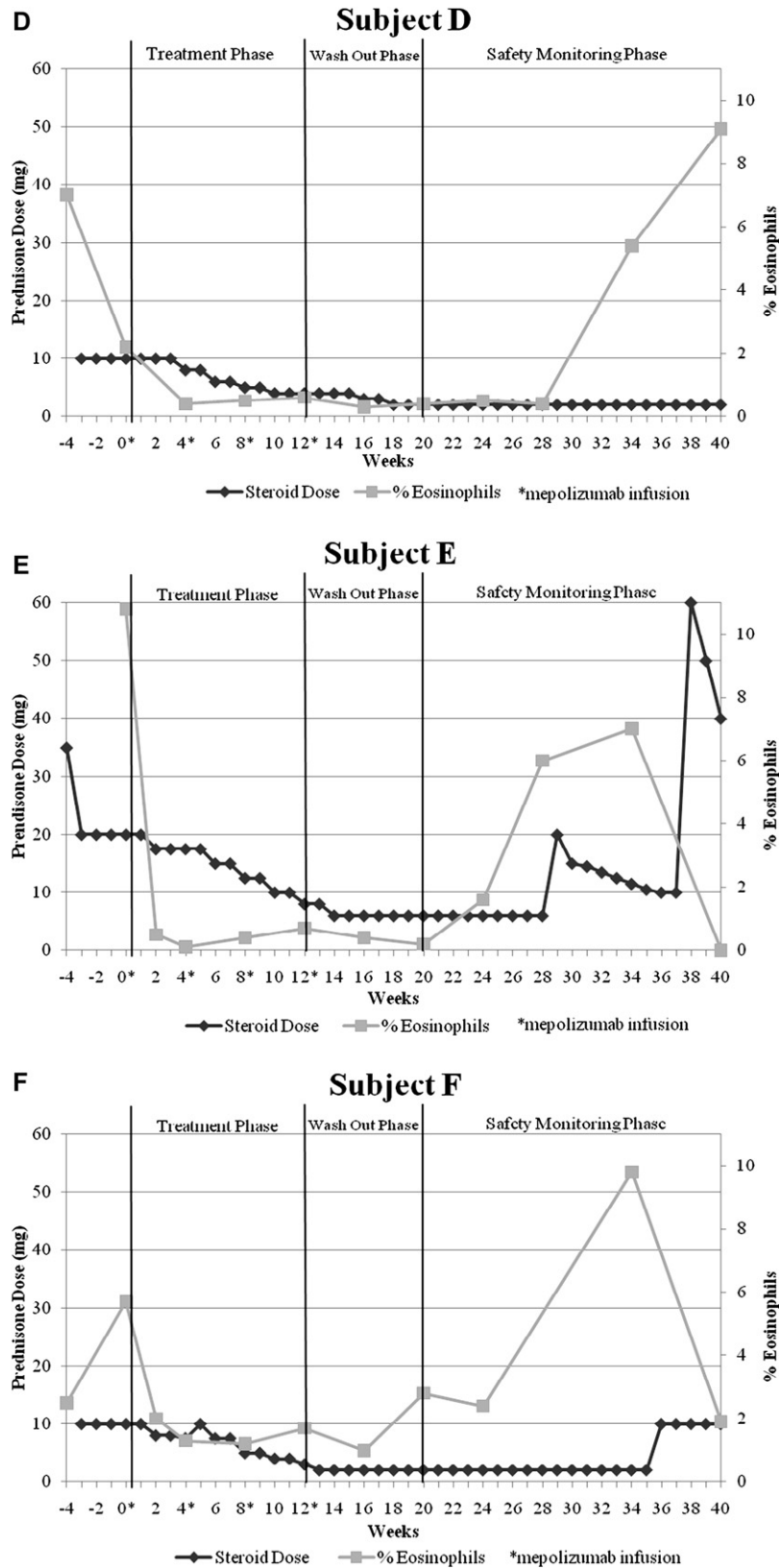


FIG 2. (Continued)

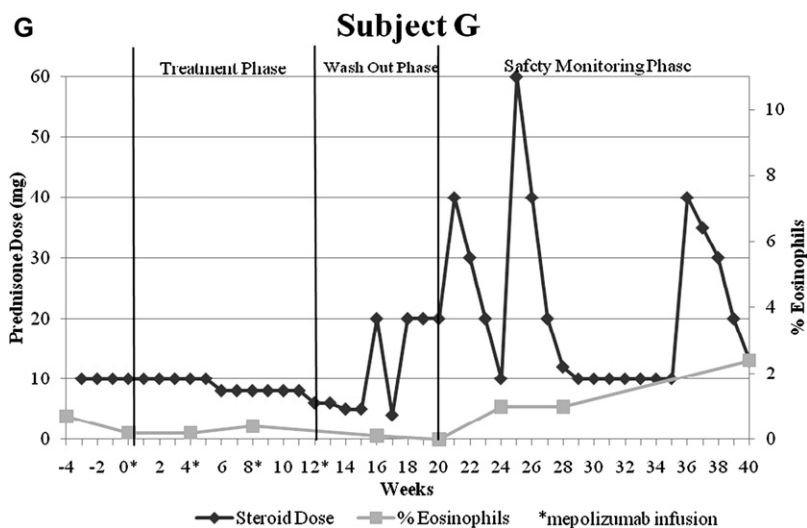


FIG 2. (Continued)

TABLE II. Summary table of outcome variables in all 7 patients at different times throughout the study

Mean (range)	Week -4, enrollment	Week 0, treatment phase	Week 12, treatment phase	Week 16, washout phase	Week 20, washout phase	Week 28, safety-monitoring phase	Week 40, safety-monitoring phase
Prednisone dose (mg)	18.8	12.9	4.6	6.7	5.0	4.3	15.7
Eosinophil (%)	2.9 (0.2-7)	3.4 (0.1-10.8)	0.8 (0.5-1.7)	0.4 (0.1-1)	1.0 (0-2.8)	2.4 (0.4-6)	3.8 (0-9.9)
No. of exacerbations		2		4			14
IL-5 (pg/mL)	8 (2-14)	12 (0-65)	7 (0-24)	5 (0-10)	Not collected at this visit	Not collected at this visit	6 (0-18)
FEV ₁ (% predicted)	79 (60-101)	76 (59-98)	76 (49-102)	75 (47-99)	75 (52-99)	80 (47-111)	77 (47-98)
PEF	Not measured @ visit	410 (300-480)	432 (210-529)	404 (210-529)	413 (240-529)	421 (280-523)	443 (380-564)
ACQ score	1.74 (0-2.86)	1.57 (0-2.86)	1.22 (0.29-2)	1.02 (0-1.71)	1.36 (0-1.83)	1.65 (0-3.86)	1.14 (0.57-3.86)
FeNO	62.2 (15-153.4)	47.4 (11-141.7)	39.1 (9.3-101.1)	50.5 (9.7-163.7)	62.1 (20.5-98.6)	Not collected at this visit	49.9 (31.1-86)
BVAS score	10.5 (3-18)	6.9 (3-15)	6.1 (0-11)	6.4 (0-17)	7.4 (0-14)	9.3 (3-12)	8.0 (0-23)
CRP (mg/L)	6.2 (0.6-15.8)	3.9 (0.8-10.5)	6.1 (0.9-17.1)	4.2 (0.8-19.3)	7.5 (0.8-27.4)	3.1 (0.8-12.4)	6.5 (0.4-19.6)
ESR (mm/h)	8 (2-25)	7 (2-20)	10 (3-21)	9 (2-25)	11 (1-26)	4 (1-6)	7 (2-27)

There were no significant changes in markers of disease activity noted despite clinical stability and decreased overall prednisone dosing. Mean IL-5 levels did not change in response to mepolizumab therapy.

PEF, Peak expiratory flow.

required to define those factors and corroborate the findings in this pilot trial.

The route by which tissue injury occurs in patients with CSS is unclear. However, the considerable eosinophilia (>10%) that distinguishes this syndrome from other vasculitides appears to play a key role. The mechanism by which the eosinophilia develops and persists is also uncertain. However, patients with CSS have been shown to demonstrate increased bone marrow release of eosinophils,¹⁷ as well as decreased peripheral destruction.¹⁸ Additionally, the cells themselves have been noted to be in an activated state, degranulating and releasing cytotoxic enzymes, resulting in local and systemic damage.^{3,19} Patients with progressive disease are noted to have significantly increased eosinophil counts in bronchoalveolar lavage fluid compared with those seen in patients with CSS in partial remission.³ This appeared to be reinforced in the cases of peripheral blood eosinophilia in our trial: patients tolerated lower steroid doses to control symptoms when eosinophil concentrations were concurrently low.

Mepolizumab binds to free IL-5 with high affinity and specificity and prevents association between IL-5 and IL-5 receptors on the surface of eosinophils.²⁰ It induces bone marrow eosinophil maturational arrest and decreases eosinophil progenitors and subsequent maturation in the blood²¹ and bronchial mucosa.²² Given that eosinophil concentrations and degranulation products are closely correlated with CSS disease status, a reduction of this pivotal player in the pathologic pathway likely results in improved clinical status.

The relationship between IL-5 and eosinophilia has been well demonstrated in models in which IL-5 transgenic mice had profound eosinophilia and IL-5-deficient mice had dramatically less eosinophilia after allergen challenge.^{23,24} In human trials mepolizumab has been shown to dramatically decrease blood eosinophil levels in asthmatic subjects^{25,26} and patients with eosinophilic esophagitis.⁶ Although reduction in peripheral eosinophilia was reproduced in asthmatic subjects by Flood-Page et al²⁷ with a significant but less extensive reduction in bone

marrow and bronchial mucosa, these effects did not translate into improvement in asthma status. More recently, however, 2 double-blind placebo-controlled trials of mepolizumab in subjects with eosinophilic asthma showed a significant decrease in severe exacerbations and improvement in quality of life.^{12,13} Similar to our study's demonstration of mepolizumab's ability to reduce corticosteroids in patients with CSS, in a double-blind placebo-controlled trial of patients with non-CSS hypereosinophilic syndromes, Rothenberg et al⁹ demonstrated that mepolizumab allowed for corticosteroid withdrawal and reduction of hypereosinophilic syndrome flares.

This pilot study proposes that adjunct therapy with mepolizumab results in clinical stability while reducing steroid dosing and reiterates the significant role of eosinophils in patients with CSS. However, the lack of improvement in lung function suggests that other pathways contribute to pulmonary compromise or that one must identify a subset of patients who have biomarkers suggestive of mepolizumab responsiveness (eg, sputum eosinophilia). In our study IL-5 levels were low and did not predict responsiveness to therapy. One limitation of this study is that the degree of eosinophilia within the airways or in other tissues was not directly assessed. To assess whether mepolizumab is effective in reducing bronchial eosinophilia, future studies could include bronchial biopsy, bronchoalveolar lavage, or evaluation of sputum eosinophils.

We recognize that the open-label design of the study can be associated with certain biases and that the small sample size makes it difficult to generalize these data to patients with CSS at large. However, because of the rarity of this disease, recruiting large numbers of patients with CSS at a single site is challenging. Furthermore, these subjects did well during therapy. It is worth reemphasizing that subjects remained clinically stable with these substantially decreased steroid doses despite prior attempts with alternative adjunct therapies. These data suggest that mepolizumab is safe and efficacious in patients with CSS; however, a larger, randomized, double-blind placebo-controlled trial is now needed to substantiate these findings. It could include patients with CSS whose conditions are unstable at baseline doses of less than 10 mg/d prednisone. Given the rarity of this disease, multiple centers will likely be required to recruit a sufficient number of subjects with this rare disease. Given the substantial burden that patients with CSS carry and the side effects of current therapies, mepolizumab has potential as a safe disease-modifying agent; it could change our approach to this rare disease and improve our patients' quality of life.

Clinical implications: Mepolizumab allows for safe steroid tapering while maintaining clinical stability and appears to be a viable therapeutic option in patients with CSS.

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APPENDIX 1. Prednisone taper schedule

If you currently take 55 or more mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

50 mg for 2 weeks then
40 mg for 2 weeks then
30 mg for 2 weeks then
20 mg for 2 weeks then
17.5 mg for 2 weeks then
15 mg for 2 weeks then
12.5 mg for 2 weeks then
10 mg for 2 weeks

If you currently take 45-54 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

40 mg for 2 weeks then
30 mg for 2 weeks then
20 mg for 2 weeks then
17.5 mg for 2 weeks then
15 mg for 2 weeks then
12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks

If you currently take 40-44 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

35 mg for 2 weeks then
30 mg for 2 weeks then
20 mg for 2 weeks then
17.5 mg for 2 weeks then
15 mg for 2 weeks then
12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks

If you currently take 35-39 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

30 mg for 2 weeks then
20 mg for 2 weeks then
17.5 mg for 2 weeks then
15 mg for 2 weeks then
12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks then
6 mg for 2 weeks

If you currently take 30-34 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

25 mg for 2 weeks then
20 mg for 2 weeks then
17.5 mg for 2 weeks then
15 mg for 2 weeks then
12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks then
6 mg for 2 weeks

If you currently take 25-29 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

20 mg for 2 weeks then
17.5 mg for 2 weeks then
15 mg for 2 weeks then
12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks then
6 mg for 2 weeks then
5 mg for 2 weeks

If you currently take 20-24 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

17.5 mg for 2 weeks then
15 mg for 2 weeks then

APPENDIX 1. (Continued)

12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks then
6 mg for 2 weeks then
5 mg for 2 weeks then
4 mg for 2 weeks

If you currently take 15-19 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

12.5 mg for 2 weeks then
10 mg for 2 weeks then
8 mg for 2 weeks then
6 mg for 2 weeks then
5 mg for 2 weeks then
4 mg for 2 weeks then
3 mg for 2 weeks then
2 mg for 2 weeks

If you currently take 10-14 mg of prednisone per day, starting 2 weeks after your first mepolizumab infusion, decrease to:

8 mg for 2 weeks then
6 mg for 2 weeks then
5 mg for 2 weeks then
4 mg for 2 weeks then
3 mg for 2 weeks then
2 mg for 2 weeks then
1 mg for 2 weeks then
0 mg for 2 weeks

(Continued)