

The effects of an anti-CD11a mAb, efalizumab, on allergen-induced airway responses and airway inflammation in subjects with atopic asthma

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Background: Efalizumab is a humanized IgG₁ mAb against the lymphocyte function antigen-1 (LFA-1) alpha chain, CD11a. Blocking of LFA-1/intercellular adhesion molecule interactions could inhibit asthmatic inflammation by blocking adhesion and activation of LFA-1-positive leukocytes.

Objective: A randomized, double-blinded, placebo-controlled, parallel group, multicenter study investigated the effects of efalizumab on allergen-induced airway responsiveness and airway inflammation.

Methods: Thirty-five nonsmoking subjects with mild allergic asthma were randomized to receive efalizumab ($n = 24$) or placebo ($n = 11$) in 8 weekly subcutaneous doses (0.7 mg/kg conditioning dose followed by 7 weekly doses of 2.0 mg/kg). Allergen challenges were performed at screening and after 4 and 8 weeks of treatment. Samples of sputum ($n = 18$ subjects) and blood ($n = 35$ subjects) were collected the day before challenges, and sputum was collected again at 7 and 24 hours after each challenge. Nonparametric tests were used to compare allergen-induced differences between efalizumab and placebo groups.

Results: Subjects receiving efalizumab developed headache (48%) and flu syndrome (28%) compared to subjects receiving placebo (0%). After 8 weeks of efalizumab, the maximum late percent fall in FEV₁ (late asthmatic response) was inhibited by 50%, but neither the late response nor the late area under the curve was statistically different than placebo ($P = .098$ and $.062$, respectively). Efalizumab had no effect on the maximum early percent fall in FEV₁ (early asthmatic response) or early area under the curve compared to placebo ($P > .59$). Efalizumab significantly reduced the postallergen increase in sputum EG2-positive cells and metachromatic cells ($P < .05$). No other comparisons were statistically different.

Conclusions: Blocking of LFA-1/intercellular adhesion molecule interactions by efalizumab inhibits the development of allergen-induced cellular inflammatory responses measured in induced sputum and might attenuate the late asthmatic response. Larger studies are needed to confirm this. (J Allergy Clin Immunol 2003;112:331-8.)

Key words: Sputum eosinophils, allergen inhalation challenge, anti-CD11a antibody, LFA-1

Inhalation of allergen by subjects with atopic asthma is associated with acute bronchoconstriction, which in approximately half of subjects is followed by a late airway bronchoconstriction.¹ The early response is mainly caused by immediate release of mast cell products, whereas the late airway response is accompanied by airway hyperresponsiveness² and airway inflammation. This allergen-induced inflammation is characterized by an influx of effector cells, such as eosinophils, mast cells, and basophils, which have been shown to increase in airway tissue³ and bronchial secretions.⁴⁻⁶ Although short-term treatment with β -agonist can reduce the maximum early (EAR) and late (LAR) percent fall in FEV₁ after allergen challenge, there are inconsistent effects on inhibition of airway inflammation.⁷ Furthermore, regular treatment with β -agonist can worsen the LAR⁸ and associated airway inflammation.⁹ Inhaled steroids effectively inhibit the LAR and only partially suppress allergen-induced airway inflammation.¹⁰ Presently, there is a need for an asthma therapy that is capable of inhibiting airway responses and airway inflammation.

The T lymphocyte appears to be central to the development of allergic airway inflammation by producing T_H2 cytokines, which support activation of these effector cells at the site of inflammation. The adhesion molecule, lymphocyte function antigen-1 (LFA-1), might be critical for the development of allergic inflammation, because it appears to play a major role in T-lymphocyte adhesion to vascular endothelium,¹¹ cytotoxic function,¹² and activation.¹³ A humanized mAb to CD11a (the alpha chain of LFA-1), which has been studied as a therapy for psoriasis, has recently been shown to be effective in reducing numbers of epidermal and dermal CD3⁺ T lymphocytes in patients with moderate to severe psoriasis.¹⁴ Blocking of

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Funding for this study and the study drug were provided by Genentech Inc, South San Francisco, Calif.

Received for publication May 6, 2003; revised May 26, 2003; accepted for publication June 3, 2003.

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0091-6749/2003 \$30.00 + 0

doi:10.1067/mai.2003.1689

Abbreviations used

AUC:	Area under the curve
DR:	Dual responder asthmatic
EAR:	Maximum early % fall in FEV ₁
GSEM:	Geometric standard error of the mean
ICAM:	Intercellular adhesion molecule
IER:	Isolated early responder asthmatic
LAR:	Maximum late % fall in FEV ₁
LFA-1:	Lymphocyte function antigen-1
VLA-4:	Very late antigen-4

LFA-1 or its ligand, intercellular adhesion molecule-1 (ICAM-1), is effective in blocking the EAR, LAR, and allergic inflammation in rats^{15,16} and mice.^{17,18} This raises the possibility that regulation of migration and activation T lymphocytes and other LFA-1-positive leukocytes, such as eosinophils and basophils, might suppress the allergen-induced bronchoconstrictor response and T_H2-driven allergic inflammation in subjects with allergic asthma. We hypothesized that blocking of LFA-1 would also be effective in blocking the LAR, which is associated with airway inflammation of subjects with atopic asthma after allergen inhalation challenge. In the current study, we investigated the safety and efficacy of this CD11a antibody, efalizumab, in a human model of atopic asthma.

METHODS**Subjects**

Thirty-seven subjects were enrolled in the study. One subject dropped out of the study before receiving study drug because of scheduling difficulties, and one subject dropped out of the study after the conditioning dose because of adverse events. Thirty-five subjects, 23 male/12 female, age 18 to 60 years old (mean, 31 years old), completed the study. Inclusion criteria required subjects to be non-smokers with mild atopic asthma, free of other lung disease, and no history of recurrent bacterial, viral, or fungal infection. Although efalizumab would be anticipated to have beneficial effects in severe asthma, subjects with mild asthma were recruited for allergen inhalation and subsequent evaluation of the allergen-induced airway inflammation. Subjects were required to have stable asthma with FEV₁ greater than 70% of predicted on all study days before allergen challenges, baseline methacholine PC₂₀ of 16 mg/mL or less, to use no regular asthma medication during the study other than infrequent (less than twice weekly) inhaled β_2 -agonist, which was withheld for 8 hours before each visit, to have no exposure to sensitizing allergens apart from house dust mite, to have no asthma exacerbations or respiratory tract infections for 4 weeks before entering the study, and to refrain from rigorous exercise, tea, or coffee in the morning before visits to the laboratory.

Study design

A multicenter, double-blinded, placebo-controlled (2 efalizumab:1 placebo), randomized, parallel group study was carried out. Thirty-five subjects with allergen-induced isolated early responses (IER; an LAR less than 15% fall in FEV₁ 3 to 7 hours after allergen challenge) or dual airway responses (DR; an LAR of 15% or greater fall in FEV₁ 3 to 7 hours after allergen challenge) were enrolled between December 1999 and May 2000 by 1 of 4 centers and were randomized by using a centralized, stratified system resulting in the following distribution: 24 DR (n = 16 efalizumab, n = 8 placebo) and

11 IER (n = 8 efalizumab, n = 3 placebo) (Fig 1). The random allocation sequence was implemented by using a central telephone system and was concealed until interventions were assigned. The study was approved by the ethics research board of the respective institutions, and signed informed consent was given to participate. Screening of subjects included a detailed history, physical examination, chest radiograph, allergen skin test, measurements of FEV₁, methacholine PC₂₀, and diluent and allergen inhalation challenges. A physical examination was carried out during each visit to the laboratory. Subjects reported to the laboratory 8 consecutive weeks for injection of efalizumab or placebo (Fig 2). All data were obtained in the clinical laboratory. Immediately before injection, blood was drawn for measurements of serum chemistry, drug kinetics, complete blood cell count, and antibodies to efalizumab. Subjects underwent 3 allergen challenges: (1) screening, (2) after 4 weeks, and (3) after 8 weeks of treatment (Fig 2). Baseline measurements of FEV₁ and PC₂₀ were determined the day before allergen inhalation challenge. Allergen was inhaled the following morning, and the FEV₁ was measured at intervals for 7 hours after challenge. FEV₁ and PC₂₀ were determined 24 hours after challenge. In 18 subjects from 2 of the centers (n = 13 drug, n = 5 placebo), sputum was induced 24 hours before and again 7 and 24 hours after each allergen challenge for measurement of inflammatory cells (Fig 1). Subjects returned for a follow-up visit 78 days after receiving the first treatment dose.

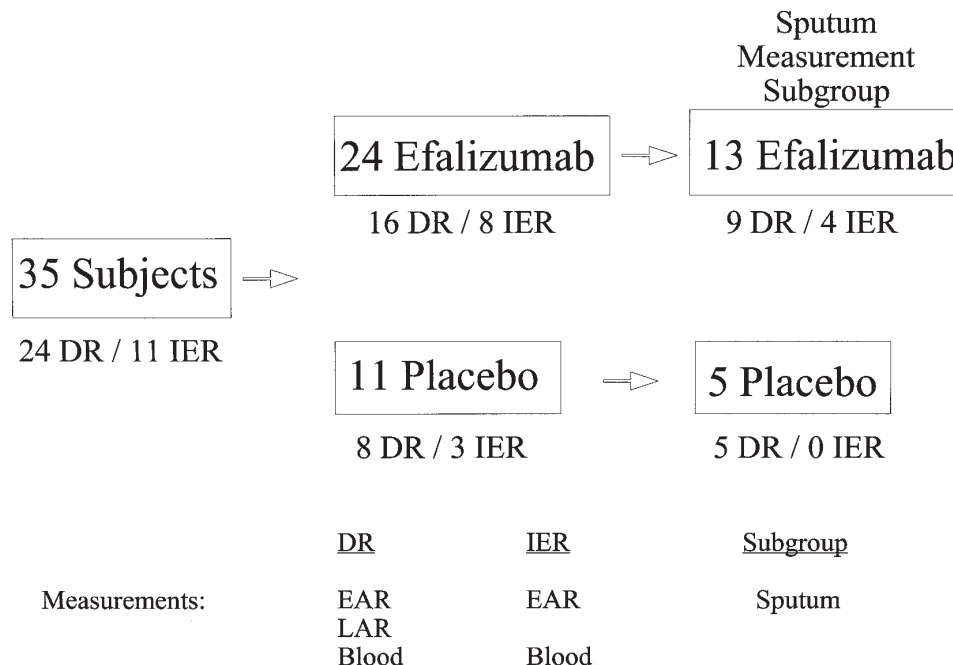
Laboratory procedures

Drug injection. Drug was supplied as a lyophilized powder containing L-histidine, beta-beta-trehalose, and polysorbate and reconstituted in sterile water to a concentration of 100 mg/mL. Placebo had the same composition without immunoglobulin. Drug was administered by using aseptic subcutaneous injection in alternating forearms with a conditioning dose of 0.7 mg/kg the first week and increased to 2.0 mg/kg for all 7 subsequent administrations.

Methacholine inhalation test. Methacholine inhalation challenge was performed as described by Cockcroft.¹⁹ Subjects inhaled normal saline during 2 minutes of tidal breathing and nebulized at 0.13 mL/min from a Wright nebulizer (Roxon Medi-Tech LTD, Montreal, Quebec, Canada), then doubling concentrations of methacholine phosphate. FEV₁ was measured at 30, 90, 180, and 300 seconds after each inhalation. The test was terminated when a fall in FEV₁ of 20% of the baseline value occurred, and the methacholine PC₂₀ was calculated.

Allergen inhalation challenge. Allergen challenge was performed as described by O'Byrne et al.¹ Subjects were skin tested for allergies to common aeroallergens. The allergen producing the largest skin wheal diameter was diluted in 0.9% saline and stored for subsequent allergen inhalation challenges. These allergens were mixed grass (n = 10), cat pelt (n = 9), house dust mite (n = 8), ragweed (n = 3), birch (n = 3), and horse (n = 2). The concentration of allergen extract for inhalation was determined from a formula described by Cockcroft et al,²⁰ and doubling concentrations of allergen were given until a 15% or greater early fall in FEV₁ at 10 minutes after allergen was reached. The FEV₁ was then measured at regular intervals until 7 hours after allergen inhalation. The EAR is the maximum % fall in FEV₁ within 2 hours after allergen inhalation, and the LAR is the maximum % fall in FEV₁ between 3 and 7 hours after allergen inhalation. The early area under the curve (AUC_{0-2h}) and the late area under the curve (AUC_{3-7h}) were calculated by using graphics software (FigP, FigP Software Corporation, Durham, NC). Subjects inhaled the same dose of allergen during screening and at week 4 and week 8.

Sputum analysis. Sputum was induced and processed by using the method described by Pizzichini et al.²¹ Cell plugs were selected and mixed with 0.1% dithiothreitol (Sputolysin; Calbiochem Corp, San Diego, Calif) and Dulbecco's phosphate buffered saline (Life Technologies Inc, Grand Island, NY) and filtered through a 52- μ m



Asthma, rhinitis, other
respiratory diseases

FIG 1. Double-blinded randomization scheme. Thirty-five subjects were randomized with 24 subjects having dual airway responses and 11 having isolated early airway responses to inhaled allergen. Subgroups (at right) are those subjects with induced sputum collections. Analyses performed are at the bottom of the figure.

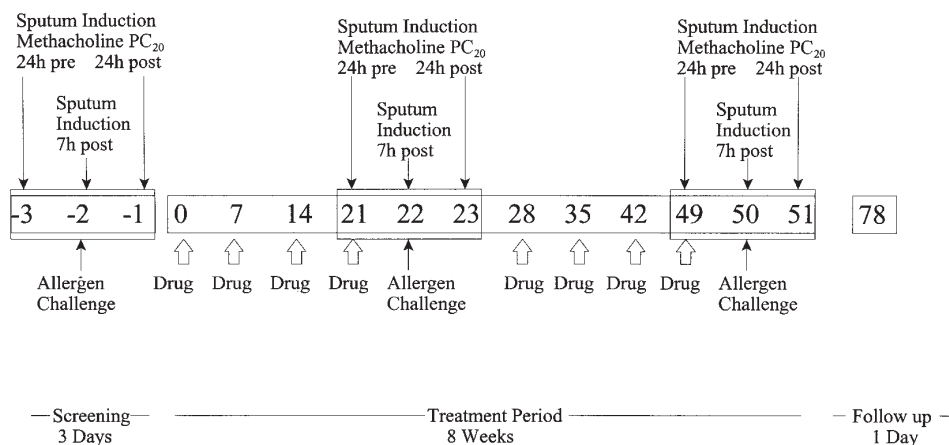


FIG 2. Study schematic showing screening period (days -3 to -1), treatment period (days 0 to 51), and follow-up period on day 78. Subjects underwent 3 allergen challenges, and FEV₁ was measured until 7 hours after challenge. Methacholine PC₂₀ was measured the day before and the day after challenges. Sputum was induced the day before and 7 and 24 hours after challenge.

nylon gauze (BNSH Thompson, Scarborough, Ontario, Canada), and cytopins were prepared on glass slides. The total cell count was determined by using a Neubauer hemocytometer chamber (Hausser Scientific, Blue Bell, Pa) and expressed as the number of cells per milliliter sputum. Differential cell counts were obtained from slides stained with Diff Quik (American Scientific Products, McGaw Park, Ill), and metachromatic cells (mast cells and basophils) were enumerated on slides stained with toluidine blue. Cytopins (Shandon III cytocentrifuge, Shandon Southern Instruments, Sewickley, Pa) were also prepared on aptex-coated glass slides and in periodate-lysine-paraformaldehyde for immunocytochemical staining of activated eosinophils (EG2) (Kabi Pharmacia, Uppsala, Sweden) and lymphocytes (CD3) (Becton Dickinson, San

Diego, Calif) by using the alkaline phosphatase antialkaline phosphatase method (DAKO, Glostrup, Denmark). Negative isotype controls (murine IgG₁; Sigma Chemical Co, St Louis, Mo) were included for each subject.

Statistical analysis

Summary statistics are expressed as mean and SEM except methacholine PC₂₀, which is expressed as geometric mean and geometric standard error of the mean (GSEM). The PC₂₀ was calculated by linear interpolation of log dose-response curves and log-transformed to fit a normal distribution before analysis. The within groups analyses were performed with Wilcoxon signed rank test, and between groups analyses were performed with rank sum tests.²²

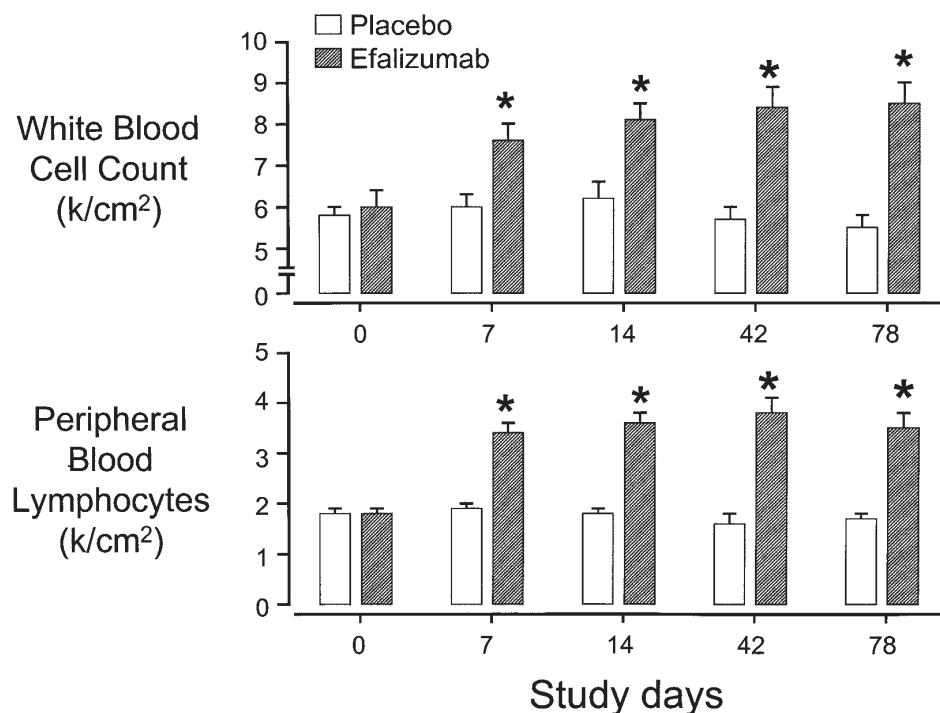


FIG 3. Mean ($\pm$ SEM) total white cells (*top panel*) and lymphocytes (*bottom panel*) measured from peripheral blood before (day 0) and after treatment with placebo (*open bars*) and efalizumab (*hatched bars*). * $P < .05$ difference between placebo and efalizumab groups.

TABLE I. Comparison of adverse events between groups

Adverse event (with frequency of $\geq 8\%$, ie, 2 or more events)	Efalizumab (n = 24)	Placebo (n = 12)
Any adverse event	76%	36%
Overall infection rate	20%	20%
Asthma adverse events	16%	27%
Flu syndrome*	28%	0%
Headache*	48%	0%
Pharyngitis	24%	18%
Bronchitis	8%	0%

* Considered by the investigator to be related to efalizumab.

RESULTS

Data from all 35 subjects were analyzed for safety and measurements of blood and spirometry. Data from the subgroup of 18 subjects were analyzed for measurements of sputum. There were no serious adverse events associated with efalizumab treatment, and no antibody production against efalizumab was detected. There were more adverse events in the efalizumab group compared with placebo (Table I); the most common adverse event associated with efalizumab was a headache and flu-like syndrome, which were transient and related to the first dose. These transient adverse events prompted 1 subject to withdraw from continued participation after a single (conditioning) dose of active drug. Maximal trough concentrations of efalizumab were measured by 3 weeks (day 21), ranging between 7 and 20 $\mu\text{g/mL}$. These levels were maintained between 7 and 40 $\mu\text{g/mL}$ until the last

day of dosing (day 49) and decreased to approximately half the peak levels during the follow-up (day 78).

The white blood cell count increased significantly after efalizumab treatment ($P < .05$) (Fig 3) as a result of increased numbers of circulating lymphocytes ($P < .05$), with no change in any other cell type.

The LAR was inhibited by 48% in the efalizumab group, $13.4\% \pm 2.7\%$ after 8 weeks of treatment compared to $25.7\% \pm 2.6\%$ at screening ($P = .001$) (Fig 4), and the $\text{AUC}_{3-7\text{h}}$ measured in the efalizumab group after 8 weeks of treatment was also significantly attenuated compared to screening ($P = .001$). The LAR was inhibited by only 18% in the placebo group, $17.9\% \pm 2.3\%$ after 8 weeks of treatment compared to $21.9\% \pm 2.6\%$ at screening ($P > .05$). The difference between the efalizumab and placebo groups did not reach statistical significance (LAR, $13.4\% \pm 2.7\%$ vs $17.9\% \pm 2.3\%$, respectively, $P = .098$, and $\text{AUC}_{3-7\text{h}}$ ($P = .062$); however, there was a

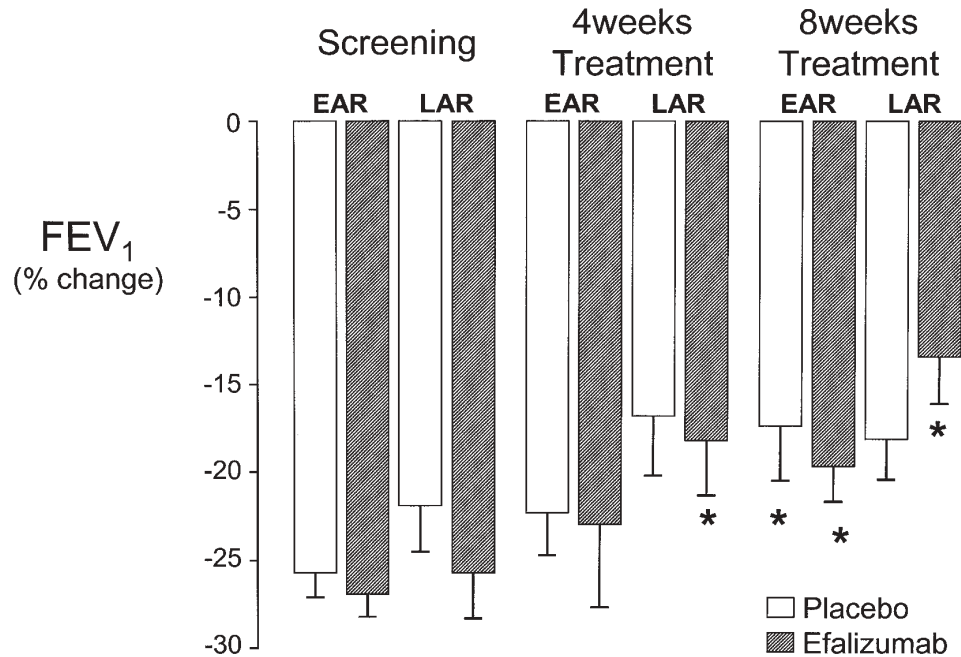


FIG 4. Mean (± SEM) percent change in FEV₁ during the EAR (0-120 minutes) and the LAR (3-7 hours) in the placebo group (open bars) and efalizumab group (hatched bars) after allergen challenges during screening and after 4 weeks and 8 weeks of treatment. *P < .05 within group difference compared to screening.

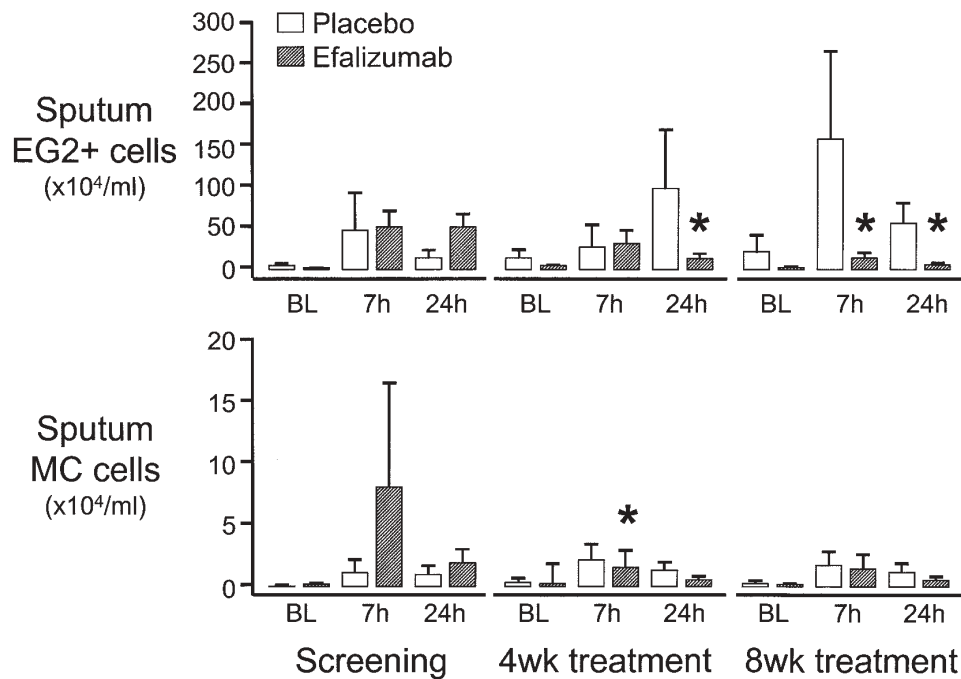


FIG 5. Mean (± SEM) number of EG2-positive cells (top panel) and metachromatic cells (bottom panel) measured at baseline and 7 and 24 hours after allergen challenges during the screening period and after 4 and 8 weeks of treatment with placebo (open bars) and efalizumab (hatched bars). *P < .05 difference between placebo and efalizumab groups.

trend toward a reduction in the late airway response with efalizumab. There was no difference between efalizumab or placebo treatment in the inhibition of the EAR or early AUC_{0-2h} (P > .05) or allergen-induced methacholine PC₂₀ (P > .05) during weeks 4 or 8.

There was no effect of efalizumab on the total number of cells in sputum (P > .05); therefore sputum cells were expressed as absolute numbers. Sputum EG2-positive cells (activated eosinophils) reached maximal levels at 7 and 24 hours after allergen inhalation (Fig 5).

After 4 weeks of treatment, the allergen-induced increase in sputum EG2-positive cells at 24 hours after allergen was significantly attenuated by efalizumab compared to placebo, $13.4 \pm 6.0 \times 10^4/\text{mL}$ compared to $98.8 \pm 71.6 \times 10^4/\text{mL}$ ($P = .006$). After 8 weeks of treatment, the allergen-induced increase in sputum EG2-positive cells was attenuated by efalizumab compared to placebo at 7 hours after allergen, $14.0 \pm 6.5 \times 10^4/\text{mL}$ compared to $158.8 \pm 107.7 \times 10^4/\text{mL}$ ($P = .002$), and at 24 hours after allergen, $6.3 \pm 2.1 \times 10^4/\text{mL}$ compared to $56.3 \pm 25.3 \times 10^4/\text{mL}$ ($P = .002$) (Fig 5). Sputum metachromatic cells were at maximal levels at 7 hours after allergen inhalation (Fig 5). After 4 weeks of treatment the allergen-induced increase in sputum metachromatic cells (mast cells and basophils) at 7 hours was attenuated by efalizumab compared to placebo, $0.54 \pm 0.28 \times 10^4/\text{mL}$ compared to $1.32 \pm 0.66 \times 10^4/\text{mL}$ ($P = .03$) (Fig 5). There was no effect of efalizumab on the number of sputum CD3⁺ cells measured by immunocytochemistry ($P > .05$).

The allergen-induced airway hyperresponsiveness measured 24 hours after allergen challenge was attenuated at weeks 4 and 8 by efalizumab compared to screening allergen challenge. In the efalizumab group, the methacholine PC₂₀ increased from 1.41 mg/mL (0.64 GSEM) at 24 hours after screening allergen challenge to 3.89 mg/mL (2.39 GSEM) at 24 hours after week 4 allergen challenge ($P = .024$) and 2.55 mg/mL (1.13 GSEM) at 24 hours after week 8 allergen challenge ($P = .001$). There was no significant effect of placebo treatment on allergen-induced methacholine PC₂₀, 1.94 mg/mL (0.98 GSEM) and 1.94 mg/mL (0.97 GSEM) after 4 and 8 weeks, respectively, compared to screening, 2.24 mg/mL (1.35 GSEM) ($P > .05$). The between group P values for efalizumab versus placebo at weeks 4 and 8 did not reach statistical significance, $P = .08$ and $.09$, respectively.

DISCUSSION

We have shown that the allergen-induced accumulation of airway eosinophils, mast cells, and basophils in subjects with asthma is significantly reduced by treatment with efalizumab, an antibody directed against CD11a (the LFA-1 alpha chain), suggesting that interactions with LFA-1 play a central role in the pathologic condition of allergic airway inflammation. The effect of efalizumab on pulmonary function measurements was not statistically significant, which suggests dissociation between airway eosinophilia and pulmonary function.

After allergen inhalation challenge, subjects treated with efalizumab had a reduction in the LAR compared to screening challenge and a reduction in the number of allergen-induced inflammatory cells as compared to subjects treated with placebo. This reduction in late airway responses to allergen after treatment with anti-LFA-1 in the current study and in studies of rats¹⁶ and mice¹⁷ demonstrates that the β integrin, LFA-1, plays a central role in the allergen-induced accumulation of airway inflammatory cells, specifically EG2-positive cells (activated eosinophils) and metachromatic cells (mast cells

and basophils), which have been shown to be associated with the LAR.⁶ The fact that the attenuation in the LAR did not reach statistical significance compared to placebo group and the reductions in the number of inflammatory cells were not observed at all time points studied might be explained by the small sample size and heterogeneity among the sample population of IER and DR subjects. The study did not have statistical power to detect 50% inhibition in this parallel-group study. However, the 48% inhibition of the LAR after 8 weeks of treatment with efalizumab demonstrates a trend for an effect, and this is the approximate degree of inhibition observed after treatment with inhaled steroid,^{10,23} which is considered by many to be the gold standard anti-inflammatory therapy for treatment of asthma. It is clear that after 8 weeks of treatment with efalizumab, there are consistent and statistically significant differences in the allergen-induced number of EG2-positive cells between the efalizumab and placebo treated groups (Fig 5), suggesting disruption of LFA-1 binding partially inhibits the accumulation and activation of LFA-1-positive effector cells such as eosinophils at the site of airway inflammation. Recent studies of allergic conjunctivitis in mice¹⁸ have demonstrated that combination therapy of anti-LFA-1 and anti-ICAM-1 is more effective in blocking allergen-induced inflammation in tissue than anti-LFA-1 alone. This is likely due to redundant functions of the integrins such as VLA-4^{24,25} and MAC-1,²⁶ which can compensate for blocking of LFA-1.

Studies of mice and humans have demonstrated that changes in pulmonary function and airway eosinophilia can occur independently.^{27,28} Our findings of significant attenuation of sputum eosinophils but only partial attenuation of the LAR are consistent with recent studies that have provided evidence that the LAR is not necessarily eosinophil-driven. The LAR has been shown to persist despite significant attenuation of sputum eosinophils with an IL-5 blocking antibody,²⁸ and the LAR provoked by intradermal injection of peptides is not accompanied by eosinophils in bronchial biopsy specimens.²⁹ Furthermore, sputum eosinophilia does not always correlate well with the degree of airway hyperresponsiveness,³⁰ particularly in subjects with longer-term asthma in whom there is no correlation found between methacholine PC₂₀ and airway eosinophils.³¹ Other factors such as presence of neutrophils³⁰ and TNF- α ³² play an important role in determining the severity of airway hyperresponsiveness, suggesting that the eosinophil alone might not be a good predictor of airway hyperresponsiveness.

The serum concentration and time course of subcutaneously administered efalizumab in the current study are consistent with those observed in a recently published study of a single intravenous dose in patients with psoriasis.^{14,33} Although we did not measure levels of CD11a in blood to confirm downregulation of receptor by efalizumab, we are confident that satisfactory levels of drug were achieved in the current study.¹⁴ We did not directly measure the effect of efalizumab on T-lymphocyte activation or adhesion; however, the observed increase in the number

of circulating lymphocytes suggests that the drug did indeed have an effect on the lymphocyte population. A similar increase in the number of circulating lymphocytes has been observed after regular treatment with antibodies to LFA-1 in previous studies of patients with psoriasis,^{24,34,35} monkeys,³⁶ rats,³⁷ and mice.²⁵ Although impairment of immune function is a theoretical concern when lymphocytes are prevented from migrating into tissue, in this small population of relatively healthy subjects receiving efalizumab for only 8 weeks, we did not observe any increase in bacterial, fungal, or viral infections. Several *in vivo* studies demonstrated the importance of LFA-1 in extravasation of lymphocytes into tissue by binding to its ligand ICAM-1²⁵ and possibly ICAM-2 on endothelial cells.³⁸ In addition, LFA-1 permits adherence of lymphocytes to high endothelial venules of peripheral lymph nodes,³⁹ while increasing lymphocyte trapping in the pulmonary vasculature of isolated rat lung through LFA-1/ICAM-1 interactions.⁴⁰ We therefore demonstrated that the drug reached the target level in the circulation, on the basis of studies on subjects with psoriasis,^{14,33} and increases in circulating lymphocytes indicate that the drug was functional in this group of atopic subjects.

Efalizumab almost certainly interferes with migration of T cells and other LFA-1-bearing inflammatory cells, such as eosinophils, to sites of inflammation through blocking the function of LFA-1.^{41,42} In addition, reduction of T-cell function and cytokine production might indirectly interfere with migration and activation of T_H2-driven effector cells. Targeting LFA-1 appears to be an interesting therapeutic approach for subjects with atopy, because eosinophils in subjects with atopic asthma show increased expression of LFA-1 compared to control subjects,⁴³ and allergen challenge results in early recruitment of blood eosinophils overexpressing LFA-1 in the first hours after allergen challenge.⁴⁴ Recent findings of coexpression of LFA-1 and ICAM-1 on conjunctival epithelial cells of atopic subjects during persistent allergen stimulation⁴⁵ suggest anti-LFA-1 antibodies might be especially therapeutic for interaction between epithelial cells and activated effector cells.

We have shown that efalizumab reduces the recruitment of inflammatory cells to the airway after allergen challenge without increasing the incidence of overall infections in these subjects. Efalizumab also appears to decrease the LAR, but a larger sample size would be needed to statistically confirm this finding. Together, these properties suggest a novel therapeutic approach for the treatment of allergic asthma. Although this therapy might not be cost-effective or as efficacious as inhaled corticosteroids for the treatment of asthma, these data provide a unique insight into the participation of LFA-1-bearing cells in the airway asthmatic response to allergic stimuli. Further studies would be needed to determine the exact target cells of the therapy (lymphocytes or other LFA-1-bearing cells) and to confirm the clinical benefit.

We gratefully acknowledge the technical assistance of Beth Davis, Lesley Stewart, Francine Deschesnes, Richard Watson, Erin Baswick, Joceline Otis, and Megan O'Connor.

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