Asthma and seasonal allergic rhinitis (SAR) are two of the most prevalent allergic disorders, affecting one of every five Americans. Asthma is an inflammatory disease associated with bronchial hyperresponsiveness of the airway. It affects seven to 20 million people per year in the U.S. Patients generally present with shortness of breath, wheezing, and coughing. Thirty-five percent to 55% of asthmatic patients have an allergic component to their disease. These patients are believed to have an immunoglobulin E (IgE)–mediated mast cell degranulation with the release of numerous immune mediators, such as histamine, leukotrienes, and prostaglandins.

An asthmatic attack develops from an inhalational challenge with an allergen. This challenge may elicit two types of reactions: an early asthmatic response (EAR) and a late asthmatic response (LAR).

An early asthmatic response is characterized by a drop in pulmonary function, reaching a nadir in 10 to 20 minutes, and is self-contained in one to two hours. A late asthmatic response is present in 50% of patients with an early asthmatic response. It usually begins four to six hours after exposure to an allergen and reaches maximum intensity in six to eight hours. A late asthmatic response may cause a persistent drop in pulmonary function for as long as 24 hours.

Current therapies for allergic asthma include fast-acting inhaled bronchodilators (β₂ receptor agonists), long-acting oral and inhaled bronchodilators, oral and inhaled corticosteroids (ICSs), inhaled mast cell stabilizers, and oral leukotriene antagonists. Most current therapies do not blunt either early or late asthmatic responses in asthmatic subjects and therefore do not prevent or minimize allergen-induced asthma attacks.

Allergic rhinitis affects about 20% of the U.S. population. This condition is manifested when a patient comes into contact with an allergen. In this case, allergens cause an immune reaction within the nasal mucosa, resulting in rhinorrhea, sneezing, nasal congestion, and postnasal drip. Mast cells within the nasal mucosa become sensitized by allergens cross-linked with IgE. Subsequent exposure to that allergen causes mast cells to release the same proinflammatory modulators, as in the case of allergic asthma.

Patients with allergic rhinitis also have early and late responses to allergens. An early response results in symptoms within minutes after allergen exposure and represents a rupture of the mast cell membrane and an influx of inflammatory mediators. The late response is manifested several hours later and represents an influx of basophils, monocytes, eosinophils, and macrophages into the area.

Current therapeutic modalities for allergic rhinitis include oral antihistamines, intranasal mast cell stabilizers, intranasal corticosteroids, and immunotherapy. The limitations of current therapies include lack of efficacy and frequent adverse effects.

Omalizumab (Xolair®, Genetech, Inc., and Novartis) is a monoclonal antibody directed against free, circulating plasma IgE. It is a novel therapeutic modality currently being investigated in the settings of allergic asthma and allergic rhinitis. Numerous clinical trials have evaluated its safety and efficacy. A biological license application has been submitted to the U.S. Food and Drug Administration (FDA) for omalizumab and is currently pending approval in these clinical settings.

**PHARMACOLOGY**

Omalizumab, formerly known as rhuMAb-E25, is a humanized monoclonal antibody of mouse origin. It recognizes IgE at the same site as the high-affinity receptor for IgE (the FcεRI binding site). Omalizumab forms a complex with free and circulating IgE and prevents IgE from binding to cell membrane receptors, resulting in inhibition of IgE-mediated proinflammatory action. Omalizumab does not bind to IgE that is already cell-bound and thus does not cause cross-linking of the antigens with IgE molecules on the cellular receptors. Therefore, omalizumab does not trigger proinflammatory cytokine release. Figures 1 and 2 depict the site of action of omalizumab and the structure of IgE.

**PHARMACOKINETICS**

The pharmacokinetic profile of omalizumab has been studied in patients with allergic asthma and allergic rhinitis via intravenous (IV), subcutaneous (SQ), and aerosolized routes of administration. Nebulized omalizumab was found to be ineffective. Facy and associates concluded that aerosolized delivery of omalizumab did not result in high enough plasma concentrations to inhibit the airway response to inhaled allergens. All other trials utilized either IV or SQ routes of drug delivery.

The onset of action of omalizumab is similar for both IV and SQ routes of administration. A significant decrease in the serum IgE level occurs within one hour of administration, with IgE levels falling from 1,000 to 7 ng/ml. A similar
degree of IgE suppression has been noted with various dosages of omalizumab.8

Omalizumab follows a one-compartment pharmacokinetic model with an apparent volume of distribution (Vd) approximating that of plasma volume.3 It has an elimination half-life (T1/2) of one to four weeks and a duration of action of two to four weeks after single and multiple intravenous doses.8,9 It may take up to two weeks for omalizumab to reach a steady state after IV or SQ administration.4 The maximum steady-state serum concentration of free and complexed omalizumab is 30.9 mg/L when the drug is given as a loading dose of 2 mg/kg intravenously, followed by six subsequent IV doses of 1 mg/kg over a 77-day course of treatment.4

**CLINICAL TRIALs**

**Allergic Asthma**

**Phase II Trials**

**The Fahy Study**5

Fahy and colleagues examined the effect of omalizumab on the early and late asthmatic responses in 19 allergic asthmatic patients in an 11-week randomized, double-blind, placebo-controlled, parallel-group trial. Patients were randomly assigned to receive either omalizumab, 0.5 mg/kg via IV infusion over five minutes, or placebo. During the first week of the trial, all patients underwent baseline allergen challenges (airway allergen diluent, airway allergen, and methacholine). The maximal decline in forced expiratory volume in one second (FEV1) from an early and a late asthmatic response was then calculated and represented baseline values. Patients were also taught to complete a diary at that time and to record peak flow, asthma symptoms, albuterol use, and nighttime awakenings. Omalizumab was administered for the next eight weeks of the trial, and the allergen challenges were repeated in the last two weeks of the trial. The allergen challenge produced a significantly lower drop in FEV1 in the omalizumab arm than in the placebo arm (P = .03 for early asthmatic responses, P = .047 for late asthmatic responses).5

**The Boulet Study**4

Boulet and colleagues studied the safety and tolerance of omalizumab and its ability to reduce the early asthmatic response in 20 adults with mild allergic asthma. This was a multicenter, randomized, double-blind, parallel-group, placebo-controlled trial with a duration of 11 weeks.

During the first visit, patients' baseline data were collected, including expiratory flows, airway responsiveness to methacholine, and cutaneous responsiveness by skin prick testing to a battery of common allergens. Serum IgE levels were also measured. Patients were randomly assigned to receive either omalizumab or placebo. The study drug was administered at a dose of 2.0 mg/kg times one dose, followed by 1.0 mg/kg every week for two weeks, and 1.0 mg/kg every other week thereafter until the end of the trial. Each dose of omalizumab was administered intravenously over five minutes into a peripheral vein. Allergen challenges and measures of serum IgE were performed throughout the study.

Nineteen patients completed the study. One patient withdrew from the trial because of urticarial rash, which developed after the first dose of omalizumab. The drug was well tolerated by all other subjects, and all other side effects were classified as infrequent and mild. Patients in the omalizumab group required higher doses of allergens and methacholine to lower their expiratory flows to baseline values than did subjects in the placebo group (P < .002 vs. P = .48). Serum IgE levels were below baseline levels in all patients in the omalizumab group, with undetectable IgE levels in 70%; no significant fluctuations in serum IgE levels were noted in the placebo group.4

**Phase III Trials**

**The Milgrom Study**9

Milgrom and associates examined the efficacy of omalizumab in patients with allergic asthma. Three hundred seventeen patients were randomly assigned to receive either one of two doses of omalizumab or placebo. Omalizumab was given either at a high dose of 5.8 mcg/kg of body weight per nanogram of IgE/ml or at a low dose of 2.5 mcg/kg of body weight per nanogram of IgE/ml. This was a randomized, placebo-controlled, double-blind, multicenter trial. All subjects had moderate to severe asthma and had to take ICSs for two months prior to the trial at a dose of at least 200 mcg of triamcinolone or equivalent.

The study consisted of four phases. During the enrollment and run-in period, patients were stabilized with an oral or

Figure 1 Site of action of omalizumab in the inflammatory cascade. (From asthma consumer information. Provided by Genentech, Inc., and Novartis Pharma. Available at: www.clearbreathing.com.6)
inhaled corticosteroid regimen. During the second phase, patients received either IV omalizumab or placebo for 12 weeks on days zero, four, and seven, and then every two weeks thereafter in addition to the corticosteroid regimen. During the third phase, an eight-week period, patients continued to receive omalizumab, but the corticosteroid dose was tapered down. The fourth phase was a 10-week follow-up period.

During the course of the study, investigators recorded asthma symptom scores, the use of inhaled beta agonists, and withdrawal of corticosteroids, and measurements of lung function by assessing peak flows. They also instructed patients to fill out asthma quality-of-life questionnaires. Serum levels of IgE were measured as well.

Scores of asthma symptoms were significantly lower in patients in both omalizumab groups compared with the placebo group (P = .005 and .008 vs. placebo). Subjects in both omalizumab groups showed a decreased use of beta agonists compared with baseline values. However, this decrease reached statistical significance only in the group receiving a high dose (P = .02). Thirty-five subjects were receiving oral corticosteroid therapy throughout the study.

During the steroid-tapering phase, 78% of subjects in the high-dose omalizumab group and 57% of subjects in the low-dose omalizumab group were able to taper down 50% of the oral steroid dose, compared with 33% of patients in the placebo group (P = .05 for the high-dose group only). The number of patients who were able to discontinue oral steroids completely was also higher in both omalizumab groups than in the placebo group, but the number did not reach statistical significance.

The percentage of ICS dose reduction was also superior in both omalizumab groups than in the placebo group. Fifty-one percent of patients in the high-dose omalizumab group and 49% of patients in the low-dose omalizumab group were able to reduce their ICS requirement by 50%, compared with 38% of patients in the placebo group (P = .07 and 0.12 vs. placebo). Eighteen percent of patients in the high-dose omalizumab group and 23% in the low-dose omalizumab group were able to stop using ICSs; only 12% of patients in the placebo group were able to discontinue ICS therapy (P < .05 for the low-dose group only).

At the end of the study, morning peak flow results were significantly higher in both omalizumab groups than in the placebo group (P = .02 and .046, respectively). Patients’ asthma quality-of-life scores were also significantly better in both omalizumab groups than in the placebo group (P < .001 and P = .007 vs. placebo).

The Solèr Study

In a multicenter, randomized, double-blind, placebo-controlled, parallel-group trial, Solèr and colleagues evaluated the efficacy, safety, and corticosteroid-sparing effect of omalizumab, administered subcutaneously in 546 patients with allergic asthma. The omalizumab dose was determined by using baseline serum IgE levels as well as body weight, and the dose had to be greater than or equal to 0.016 mg/kg of body weight per International Unit (IU) of total serum IgE/ml. For patients requiring doses of omalizumab between 150 and 300 mg, the drug was administered at four-week intervals. For patients requiring doses of omalizumab between 450 and 750 mg, the monthly dose was divided in half and administered every two weeks.

There were four phases in this study. During the run-in period, all patients were switched from ICSs to an equivalent dose of beclomethasone dipropionate (BDP). During the steroid-stable phase, the study drug or placebo was administered in addition to the established dose of BDP for 12 weeks. During the steroid-reduction phase, the BDP dose was titrated down every two weeks by 25% for eight weeks until BDP was discontinued or until asthma symptoms worsened. During the last four weeks of the trial, the lowest BDP dose required for asthma control was maintained.

Serum IgE levels were measured before and during treatment. To determine the efficacy of omalizumab, the investigators examined the number of asthma exacerbations during the steroid-stable and steroid-reduction stages of the trial. They also studied the number of patients experiencing at least one asthma exacerbation, the percent decrease in the BDP dose at the end of the steroid-reduction phase, and the use of rescue medications among patients in the omalizumab and placebo groups.

During the steroid-stable phase, the number of asthma exacerbations per patient was 0.28 for omalizumab and 0.66 for placebo. During the steroid-reduction phase, the number of asthma exacerbations per patient was 0.36 in the omalizumab group and 0.75 in the placebo group (P < .001 for both phases).

During the steroid-stable phase, 35 patients had at least one asthma exacerbation in the omalizumab group, in contrast to 83 patients in the placebo group. During the steroid-reduction phase, 43 patients in the omalizumab group, compared with 81 patients in the placebo group, had at least one asthma exacerbation (P < .001 for both phases). Seventy-nine percent of patients in the omalizumab group, compared with 55% of patients in the placebo group, were able to reduce their ICS dose by 50% (P < .001). Forty-three percent of patients receiving omalizumab were able to stop their ICS therapy completely; only 19% of patients receiving placebo were able to discontinue ICS therapy.

During the steroid-stable phase, daytime and nighttime asthma symptom scores were significantly lower in subjects taking omalizumab, and these lower scores were maintained throughout the steroid-reduction phase. The median number of puffs of rescue beta agonists was also lower in the omalizumab group versus placebo throughout the study. (P values were between <.005 and <.001 throughout different weeks of the trial.) Omalizumab was very well tolerated during this study, with the incidence of side effects comparable to that of placebo.

The Busse Study

Busse and colleagues assessed the efficacy and tolerability of omalizumab in a double-blind, placebo-controlled, multicenter, parallel-group study. During the four-week to six-week run-in period, all patients were switched from ICSs to BDP, and the dose was adjusted upward or downward to maintain previous asthma control. After the run-in period, patients were to receive omalizumab, dosed at 0.016 mg/kg x IgE (IU/ml). Thus, like the study by Solèr and coworkers, patients received either 150 mg or 300 mg every four weeks or 225 mg, 300 mg, or 375 mg every two weeks.

During the four-month steroid-stable phase, all subjects received BDP, in ad-
dition to omalizumab, at the dose that had been established during the run-in period. During the steroid-reduction phase, the steroid dose was decreased by 25% every two weeks for eight weeks until the medication was discontinued or until symptoms worsened. The investigators’ primary endpoint was the number of asthma exacerbations experienced by a patient during the steroid-stable and steroid-reduction phases.

The investigators also examined the number of patients experiencing at least one asthma exacerbation, the daily asthma symptom scores, inhaled beta-agonist use, and the pulmonary function scores along with a global evaluation of the effectiveness of treatment. Most patients who participated in this study were classified as having moderate-persistent asthma.

During the steroid-stable phase, the mean number of asthma exacerbations per patient was 0.28 in the omalizumab group and 0.54 in the placebo group \( (P = .006) \). The number of patients who experienced at least one asthma exacerbation was also significantly lower in the omalizumab group (14.6% vs. 23.3%, \( P = .009 \)).

During the steroid-reduction phase, the omalizumab group maintained significantly lower numbers of asthma exacerbations per patient (0.39 vs. 0.66, \( P = .003 \)) as well as a lower number of patients with at least one asthma exacerbation (21.3% vs. 32.3%, \( P = .004 \)). During this phase, the median dose reduction of BDP was 75% in the omalizumab group and 50% in the placebo group \( (P < .001) \). BDP therapy was discontinued completely in 39.6% of the group receiving omalizumab, in contrast to 19.1% in the group receiving placebo \( (P < .001) \).

Improvement in pulmonary function was greater throughout the study in the omalizumab group than in placebo group \( (P \) values ranged from < .001 to .019). Omalizumab was well tolerated in this trial, and the incidence of adverse events was comparable to that in patients taking placebo.11

**The Holgate Study**12

Holgate and associates examined the efficacy and safety of omalizumab in a randomized, placebo-controlled, double-blind, multicenter trial of 246 patients with severe allergic asthma. All of the subjects required very high doses of the ICS fluticasone propionate (FP) (Flovent®, GlaxoSmithKline) or an equivalent at baseline (1,000 to 2,000 mcg/day). The study design was similar to that of Soler and Busse and their colleagues.

During the four-week to six-week run-in period, all of the patients were stabilized with FP to maintain previous asthma control. After the run-in period, all subjects were randomly assigned to receive omalizumab, either 150 to 300 mg subcutaneously every four weeks or 225 to 375 mg subcutaneously every two weeks according to body weight and total serum IgE, or placebo.

During the 16-week steroid-stable phase, all patients received the study drug plus the dose of FP that had been established during the run-in phase. The FP dose was then decreased by 250 mcg/day every two weeks for the next 16 weeks of the trial. For the last four weeks of the trial, the minimum effective dose was maintained. The trial results have not yet been published in their entirety.

During the steroid-reduction phase, asthma symptom scores were consistently better in patients receiving omalizumab than in patients receiving placebo.

In the steroid-reduction phase, patients receiving omalizumab were able to taper their FP dose to a greater extent than patients receiving placebo \( (P = .001) \). Sixty-seven percent of patients taking omalizumab were able to decrease their FP dose by 750 mcg/day, compared with only 44% of patients taking placebo.12

**The Milgrom Study**13

Milgrom and colleagues13 investigated the drug’s safety, steroid-sparing effects, and impact on disease exacerbations in the treatment of childhood asthma in a double-blind, randomized, multicenter, parallel-group, 28-week trial. This study enrolled 334 males and premenarchal females between six and 12 years of age. At baseline levels, asthma was well controlled in all of the children. The ICS dose was equivalent to 168 to 420 mcg/day of BDP and as-needed rescue medication.

During the first phase (a four-week to six-week run-in period), all patients were switched to BDP, with the dose adjusted to maintain asthma control at baseline levels. The run-in period was followed by a 16-week steroid-stable phase, during which BDP was continued at the dose determined during the run-in period; in addition, the children received either omalizumab or placebo. Children who were randomly assigned to the omalizumab group received either 150 or 300 mg of omalizumab every four weeks or 225 mg, 300 mg, or 375 mg of the drug every two weeks.

During the final (steroid-reduction) phase, the BDP dose was tapered every two weeks for eight weeks until ICS therapy was completely stopped or until the asthma symptoms worsened. For the last four weeks of the study, the minimum effective dose of BDP was maintained.

At the end of treatment, 80.4% of children in the omalizumab group and 66.9% in the placebo group were able to decrease their BDP dose by at least 50%. BDP was completely discontinued in 55% of patients taking omalizumab but in only 39% of patients taking placebo \( (P = .004) \).

During the steroid-reduction phase, the number of patients with at least one exacerbation and the mean number of asthma exacerbations per patient were significantly lower in the omalizumab group than in the placebo group \( (P < .001) \) for both categories. Omalizumab was well tolerated, with no clinically evident drug-related toxicities reported in this study.13

Table 1 summarizes the study results.

**Allergic Rhinitis**

**The Casale Study**

Casale and colleagues conducted a phase II trial of safety, tolerance, and effectiveness of omalizumab in patients with ragweed-induced allergic rhinitis. This was a double-blind, placebo-controlled, multicenter trial with three treatment arms and two placebo arms.

Omalizumab was administered over 12 weeks, starting four weeks prior to the ragweed season. Patients received one of the three doses of omalizumab: 0.15 mg/kg subcutaneously, 0.3 mg/kg intravenously, or 0.5 mg/kg intravenously. The study drug or a placebo was given every week for the first two weeks and then every other week thereafter. Clemastine and phenylpropanolamine (Tavist-D® tablets, Novartis) were provided to all the participants to be used as rescue medication. No other allergic rhinitis medications were allowed.

Omalizumab was very well tolerated. The incidence of adverse events was similar in both the omalizumab and the
placebo groups. The average daily symptom scores of patients in the placebo arms were slightly higher than scores of patients in the omalizumab arms, but the difference was not statistically significant. The difference in the use of rescue medication between the treatment groups was not significantly different.3

The Adelroth Study

Adelroth and colleagues investigated the effectiveness of omalizumab in patients with birch pollen–induced seasonal allergic rhinitis in a randomized, double-blind, placebo-controlled, multicenter trial. Two hundred fifty-one patients were randomly assigned to receive either omalizumab or placebo. Patients with baseline IgE levels of 150 IU/ml or less received 300 mg of omalizumab or placebo at baseline lev-

levels greater than 150 IU/ml received 300 mg of omalizumab or placebo subcutaneously at baseline levels and then received one more dose four weeks later. Patients with baseline serum IgE levels greater than 150 IU/ml received 300 mg of omalizumab or placebo at baseline levels and then received two more doses at weeks three and six. Patients were allowed to use various antihistamines as rescue medications throughout the trial. No other allergic rhinitis medications were allowed. All subjects were required to record symptom severity scores into a daily diary during the eight-week treatment phase. Each day the patients also recorded their use of rescue antihistamines.

At the end of the treatment phase, the average daily nasal and ocular symptom severity scores were lower in the omalizumab group than in the placebo group ($P < .001$ and $P = .031$, respectively). The use of rescue antihistamines was significantly lower in patients receiving omalizumab than in patients receiving placebo ($P < .001$). Twenty-one percent of patients in the omalizumab treatment arm, in contrast to 2% of patients in the placebo arm, reported that the treatment completely controlled their rhinitis symptoms. Improvement in symptoms was reported in 59% of patients receiving omalizumab but only in 35% of patients receiving placebo.

Omalizumab was well tolerated in this study. There were no anaphylactic, anaphylactoid, or other serious adverse reactions to the study drug. No anti-omalizumab antibodies were detected.

The Casale Study

Another trial by Casale and associates aimed to assess the efficacy of omalizumab for the prophylaxis of symptoms of ragweed-induced seasonal allergic rhinitis. In this double-blind, placebo-controlled, dose-ranging, multicenter trial, 536 patients were randomly assigned to receive either omalizumab or placebo. Patients with baseline IgE levels between 151 and 700 IU/ml received 50 mg, 150 mg, or 300 mg of omalizumab every three weeks, for a total of four doses. Patients with baseline IgE levels below 150 IU/ml received one of these three doses of the study drug every four weeks, for a total of three doses. All patients were allowed to use chlorpheniramine maleate (ChlorTrimeton®) as their rescue antihistamine.

Each evening during the study, patients were required to record self-assessed symptom severity and duration scores. The investigators recorded the number of chlorpheniramine tablets taken by the patients each day.

Patients in the omalizumab 300-mg treatment arm had significantly lower average nasal and ocular symptom severity and duration scores than patients in the

<table>
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<tr>
<th>Table 1 Phase II Trials of Omalizumab in Allergic Asthma with a Focus on Steroid-Sparing Effects</th>
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<td><strong>Trial</strong></td>
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<td>Milgrom et al.9</td>
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<td>Soler et al.10</td>
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<td>Busse et al.11</td>
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<tr>
<td>Holgate et al.12</td>
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<td>Milgrom et al.13</td>
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* Data are presented as omalizumab versus placebo.

BDP = beclomethasone dipropionate; DB = double-blind; FP = fluticasone propionate; ICS = inhaled corticosteroid; IgE = immunoglobulin E; IV = intravenously; MC = multicenter; MP = moderate-persistent asthma; N/A = not available; NS = not significant; PC = placebo-controlled; PG = parallel-group; R = randomized; SP = severe-persistent asthma; SQ = subcutaneously; TML = triamcinolone.
The Kuehr Study

Kuehr and colleagues evaluated the effect of omalizumab in combination with specific immunotherapy (SIT) in comparison with SIT alone in children and adolescents with moderate-severe seasonal allergic rhinitis. SIT consists of administering allergen in small quantities prior to the allergy season to patients in whom this particular allergen causes the rhinitis symptoms. This study used two types of allergens as part of the SIT protocol: birch and grass (designated SIT-birch and SIT-grass).

In this randomized, double-blind, placebo-controlled, parallel-group, multicenter trial, 225 children and adolescents between six and 17 years of age were randomly assigned to one of the four treatment groups. For at least 14 weeks before the pollen season, two of the groups received SIT-birch and the other two received SIT-grass at weekly intervals by SQ injection. These 14 SIT build-up treatments were followed by another five maintenance injections of SIT at four-week intervals. Omalizumab or placebo was given to all the subjects at the same time as the maintenance SIT injections and also at four-week intervals at a dose greater than or equal to 0.016 mg/kg per IU/mL of IgE for four weeks.

Investigators assessed the patients’ daily symptom severity scores and rescue medication usage during the pollen season. The primary efficacy variable was the daily symptom load, which was calculated as the sum of the mean daily symptom severity score plus the mean daily rescue medication usage score. All adverse events were recorded and monitored.

Throughout the entire pollen season, the daily symptom load reduction was greater in both the SIT plus omalizumab groups and in the SIT plus placebo groups ($P < .001$). The proportion of days during which rescue medications were used was significantly lower in the SIT plus omalizumab groups than in the SIT plus placebo groups ($P < .001$).

During the birch pollen season, the SIT-grass group was considered a control; throughout the grass pollen season, however, the SIT-birch group was used as a control. For the duration of birch season, the SIT-birch plus omalizumab group had a 50% symptom load reduction, compared with the SIT-birch plus placebo group ($P = .003$).

Unexpectedly, during the birch season, the SIT-grass plus placebo group experienced better symptom load reduction than the SIT-birch plus placebo group. Throughout the grass pollen season, the addition of omalizumab to the SIT-birch (control) group resulted in a symptom load reduction of 45% ($P < .001$). The combination of the SIT-grass with omalizumab had a 71% symptom load reduction, compared with the SIT-birch plus placebo group. The investigators concluded that SIT and omalizumab were very well tolerated and that both modalities in combination were more effective than immunotherapy alone.

### adverse reactions

The most commonly reported adverse event was an urticarial rash, with an incidence of 0.5% to 7%. The rash developed rapidly, usually within one hour of receipt of the first dose, and responded to antihistamine therapy (i.e., IV diphenhydramine [Benadryl®, Pfizer]). Other adverse events associated with omalizumab therapy were headache, fatigue, and vertigo. There were no reports of anaphylactic reactions, and no antibodies to omalizumab were ever detected in the current studies.

### dosing and administration

#### allergic asthma

Omalizumab should be administered subcutaneously every two or four weeks at a dose greater than or equal to 0.016 mg/kg of body weight per IU of total serum IgE/mL. Doses less than 300 mg should be administered every four weeks. Patients requiring doses greater than 300 mg should receive the total four-week dose at two-week intervals (Table 2).

#### allergic rhinitis

In the clinical trials, administration of omalizumab was usually initiated before and continued throughout the pollen season. The dose varied according to the patients’ body weight and baseline serum IgE levels. Doses of 150 to 300 mg every

### Table 2 Omalizumab Dosing and Dosage Schedule

<table>
<thead>
<tr>
<th>Baseline Serum IgE (IU/mL)</th>
<th>Body Weight (kg)*</th>
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<td>30–60</td>
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*Patients weighing more than 150 kg were excluded.

** Administered every 2 weeks.

IgE = immunoglobulin E.

three to four weeks for two to four doses have shown benefit in the management of allergic rhinitis.

CONCLUSION

Omalizumab has been shown to decrease free IgE levels, resulting in reduced severity of symptoms in patients with asthma and in those with allergic rhinitis. Its use has been associated with decreased antihistamine use in patients with seasonal allergic rhinitis. The drug also has a steroid-sparing effect in patients with allergic asthma. The benefits of omalizumab have been demonstrated in adults as well as in children. Omalizumab has been well tolerated in clinical trials and has a favorable pharmacokinetic profile, allowing for once-monthly administration in most patients.

A joint new biological license application for omalizumab was submitted to the U.S. Food and Drug Administration by Genentech, Inc., and Novartis under the trade name of Xolair® in June of 2000. In July 2001, the FDA requested additional data analysis from the drug manufacturers. To address the FDA’s request, the companies have planned to submit an amendment to the biological license application in the last quarter of 2002.

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REFERENCES