Omalizumab in allergic diseases, a recent review

Pakit Vichyanond

Summary

Omalizumab is a biological engineered molecule, targeting the Cε3 domain of the IgE molecule. It binds with free IgE and prevents free IgE from attaching to high-affinity IgE receptor (FcεRI) on effector cells such as mast cells, basophils and also on dendritic cells. The result is a blocking of mediator release from these cells and the inhibition of antigen presentation by dendritic cells. In addition, omalizumab downregulates FcεRI expression on these effector cells. Omalizumab prevents early and late phase allergic reactions of skin and lungs. Omalizumab has been investigated extensively in moderate-to-severe asthma in adults and children. It effectively reduces rates of asthma exacerbation, emergency visits for asthma and hospital admissions among these patients. Currently, omalizumab is primarily indicated for patients, age 6 years and over, with moderate to severe asthma (GINA step 4). Omalizumab was investigated in patients with seasonal allergic rhinitis (to ragweed, birch and grass pollens) and has been found to improve rhinitis symptoms and to reduce medication use among these patients. Administered together with allergen immunotherapy, omalizumab reduced incidence of side effects and rates of anaphylaxis from allergen immunotherapy. Omalizumab has been investigated in the treatment of food allergy, atopic dermatitis and urticaria. Despite benefits observed from these initial trials, it further deserves investigations to clarify optimal conditions for use in these conditions. Side effects from omalizumab were few, however, it requires careful considerations in administration of this agent. An observational period (up to 2 hours after the first three doses) and the availability of auto-injectable epinephrine are recommended. Pharmacoeconomics of omalizumab is briefly reviewed. Omalizumab represents a major breakthrough of translational medicine in allergy. (Asian Pac J Allergy Immunol 2011;29:209-19)

Key words: Omalizumab, Xolair, IgE, anti-IgE, asthma, allergic rhinitis, atopic dermatitis, food allergy, urticaria

Introduction

In 1921, Prausnitz and Kustner demonstrated that immediate hypersensitivity skin reaction could be transferred from a responsive person to a nonresponsive one. Serum from Kustner (allergic to fish) was initially introduced intradermally into Prauznitz’s skin (not previously sensitized to fish). The injected site was later challenged with fish extract and yielded a positive reaction. The experiment was the first to indicate that allergic reaction was due to the presence of a substance in the blood. The substance was subsequently named ‘reagin’ which was later determined to be a heat-labile substance.
In the early 1960’s, Kimishige and Teruko Ishizaka, while working at the Children Asthma Research Institute Hospital (CARIH) in Denver Colorado, demonstrated that reagin to ragweed allergen belonged to a new class of gamma globulin, to which they named γE (E = causing erythema – K. Ishizaka, personal communication). The skin sensitizing activity of γE (to ragweed allergen) could be neutralized by an anti-III, antiserum raised against γE in animals. Simultaneously, Johansson and Bennich from Uppsala, Sweden discovered that their new myeloma protein had a property similar to globulin isolated from a dog-sensitized patient. Further screening of sera from allergic patients demonstrated high levels of this new globulin, to which they named IgND (after the name of their myeloma patient). The two groups of investigators further collaborated and finally convened at the World Health Organization in Geneva. They agreed that the two substances (γE and IgND) were identical and represented a new class of immunoglobulin. This immunoglobulin was named 1IgE.

Soon after the discovery of IgE, numerous investigations demonstrating associations between IgE and various allergic conditions, i.e., allergic rhinitis, asthma, food allergy and anaphylaxis were rapidly reported. In spite of these earlier reports, doubts remained for the association of IgE and asthma, the major prototype of immediate hypersensitivity diseases. It was in 1989 when Burrows and colleagues unequivocally reported that level of total IgE in a general population was related to the prevalence of asthma, whereas specific IgE as measured by skin tests with common allergens were associated with the prevalence of allergic rhinitis. Soon after this, Sears et al. from New Zealand reported that total level of IgE was associated with level of bronchial hyperresponsiveness in asthma. The same group later demonstrated that the degree of sensitization to house dust mites in childhood was associated with persistence of asthma into adulthood. These studies reiterated importance of IgE in the pathogenesis of asthma.

Other important finding relating the role of IgE to the pathogenesis of allergic diseases was exemplified by a study by Sampson et al. who studied the relationship of specific IgE to food substances among patients with atopic dermatitis. The investigators precisely determined the levels of specific IgE to certain foods (milk, egg, peanut, soy and wheat) that were associated with positive food challenges to these food items among these children. In short, these reports clearly indicated an intimate and causal relationship between IgE and prevalence/severity of allergic diseases.

In spite of these reports, most forms of therapy for allergic diseases prior to the turn of the century focused upon counteracting downstream products of allergic reactions such as the use of antihistamines, decongestants, bronchodilators and corticosteroids. With the advent of molecular engineering, several bioengineered molecules involved in the pathogenesis of immediate hypersensitivity reactions offered the hope of treatment targeting at the central theme of allergic reactions. Examples of these agents include anti-IgE, anti-adhesion molecules and anti-cytokines of the Th2 origin (anti-IL4 and anti-IL5). Disappointingly, of clinical studies of anti-IL5, which effectively reduced blood and sputum eosinophils, failed to inhibit the late asthmatic response and the increase in airway hyperresponsiveness. Despite the fact that the recombinant human IL-4 receptor which functions as an IL-4 antagonist was initially shown to be a promising treatment for asthma when given by means of nebulization, no further clinical development was pursued. Thus far, anti-IgE (i.e., omalizumab) is the only biotherapeutic agent that has passed through rigorous clinical trials and has been approved for the mainstream asthma therapy.

This review is intended to give readers sufficient background information about omalizumab and its use in allergic diseases. For those with further interests, in-depth reviews should be consulted.

**IgE, and IgE receptors**

IgE is a distinct class of immunoglobulin with a molecular weight of 190 kDa, and a sedimentation coefficient of 7.0 s. Its molecular structure, similar to those of other classes of immunoglobulins, comprises two heavy and two light chains (κ - kappa and λ - lambda chains). The four chains form important structures of 2 Fab’s and 1 Fc fragments. The constant Fc fragment of IgE (Ce) comprises 5 domains with domain number #3 (Ce3) being the site where IgE combines with high-affinity IgE receptors (FceRI). FceRI is a heterodimer structure consisting of 5 globular protein structures. The IgE combining site of FceRI resides in the two extracellular α chains. Mast cells and basophils are the major effector cells possessing large amount of FceRI on their cell surfaces; interactions between IgE and FceRI further upregulates FceRI expression on...
Omalizumab in allergic diseases

211

Figure 1. Binding of IgE (at Cε3) to α-chains of high-affinity IgE receptor (FCεRI) (adapted from Holgate with permission).

Figure 2. Structure of omalizumab. Omalizumab is a recombinant humanized monoclonal antibody composed of 95% human sequence and 5% murine sequence. (from Boushey et al. with permission)

these cells. Five amino acids of the Cε3 domain of IgE form a systematic three loop structure which binds tightly with α chains of the FcεRI (Figure 1.). Besides, FcεRI can also be found on several other cell types such as eosinophils, monocytes and dendritic cells. Binding between IgE and FcεRI are of high affinity and bridging of the two bound IgE molecules on surface of these effector cells lead to activation and degranulation of effector cells and thus, to the manifestations of allergic reactions. The reactions of IgE/ FcεRI on dendritic cell lead to an increased capacity of these cells in presenting allergens to T and B cells.

Anti-IgE - Omalizumab

The idea of neutralizing IgE effect started with the discovery of IgE since both the Ishizakas and Bennich-Johannson groups produced anti-IgE and used them in their earlier experiments. However, these antibodies were of animal origins and this precluded their use in human because of the possibility of generating an anaphylactic reaction. In 1993, Presta with a group of researchers at the Genetech laboratory using bioengineering techniques, produced a series of humanized anti-IgE’s which binds with IgE receptors as its original murine construct. These antibodies are of IgG1 subclasses and contain protein of 95% human origin fused with 5% mouse protein, mainly at the Fab region. Such fusion was intended to reduce the incidence of anaphylaxis when use in human. Moreover, the Fab of these antibodies is directed to Cε3 of IgE (binding site to FcεRI) and thus only bound to free IgE but not to cell-fixed IgE. Such a reaction therefore prevents bridging of FcεRI and thus does not lead to degranulation. One of these humanized antibodies further demonstrated to have desirable anti-IgE properties was omalizumab.

Omalizumab is a humanized monoclonal antibody (mab) with a molecular weight of 149 kDa. Its structure is depicted in Figure 2. Omalizumab forms a biologically inert molecule with free IgE. Omalizumab inhibits the reactions between anti-IgE and IgE sensitized mast cells and thus inhibits release of mediators and production of cytokines such as IL-13 from these cells. With appropriate dosing of omalizumab, levels of free IgE rapidly reduce to nearly zero. This effect is maintained for at least 4 months with a gradual return of level of IgE. Surprisingly, in addition to the reduction of free IgE, administration of omalizumab leads to a downregulation of FcεRI on effector cells (mainly mast cells and basophils) and also on dendritic cells. This can be viewed as an augmentation loop of the effect of omalizumab, further neutralizing effects of IgE.

Translating these cellular effects into clinical efficacy, omalizumab was shown to reduce allergen-induced early and late phase reactions both in skin-challenged and lung-challenged models. Treatments with omalizumab in allergic subjects inhibited intradermal skin tests both in the early
phase (24%) and the late phase (63%) whereas the suppression of the early-phase asthmatic response (80%) was greater than that of the late-phase response (65%). In patients with allergic asthma treated with omalizumab, a reduction of infiltrated T and B cells as well as eosinophils was noted at the submucosal layer of the bronchus. This was perhaps due to a decrease in local production of cytokines from mast cells involved in chemotaxis and survival of eosinophils in the airways such as IL-5.

**Clinical application and main indication of omalizumab**

The arrival of an anti-IgE offered a new hope for the treatment of allergic diseases, particularly for those with life-threatening situations and those in which available modes of therapy offer unsatisfactory results. One early formulation of anti-IgE, the TNX-901, was tried in the treatment of peanut anaphylaxis, the most serious food-induced anaphylaxis. The results of the study were promising, however were not sufficiently appealing enough for clinical applicability (see below). The TNX-901 was not selected for further clinical development.

Asthma is another major IgE-mediated condition which can lead to significant morbidity and the possibility of fatality in severe cases. Recently, large surveys from various parts of the world such as North America, Europe and Asia indicated that a large numbers of asthmatics could be classified in the moderate to severe persistent category. These patients were observed to suffer from serious morbidity such as persisting nocturnal symptoms, needs for extra clinic visits, and needs for hospitalization. In a large carefully conducted trial using high-dose of inhaled corticosteroids (the GOAL – Global Optimal Asthma Control study), 30% of severe persistent asthmatic patients randomized to receive a combination therapy with long-acting beta-agonist (salmeterol) and high-dose inhaled corticosteroid (fluticasone) failed to attain a status of adequate ‘asthma control’. Moreover, the cost of therapy (direct and indirect costs) for these severe asthmatic patients was 2-3 times higher than for those with mild to moderate severity. Taken together, there is a need to improved therapy for these patients and omalizumab was seen as a rational agent to be examined as an alternative or an add-on agent for this group of patients.

Omalizumab was extensively investigated in moderate-to-severe asthmatic adults. Asthma exacerbations, emergency visits due to asthma exacerbations and hospital admissions were examined as clinical outcomes examined in most studies. In the classic INNOVATE study (INvestigatioN of Omalizumab in seVere Asthma TreEatment study), 409 patients with GINA step 4 therapy (inadequately controlled with high-dose inhaled corticosteroids and long-acting beta-agonists) were randomized to receive either omalizumab (209 patients) vs placebo (210 patients). Omalizumab was administered subcutaneously at a dosage of 0.016 mg/kg per IU/ml of IgE every 2-4 weeks according to patients’ body weight and baseline IgE levels. The treatment period spanned 28 weeks. In the omalizumab-treated group, clinically significant exacerbations (adjusted for base exacerbation rate) was reduced by 26% as compared to placebo (0.68 vs 0.91, p = 0.042). Total emergency visits in the treated-group were reduced by 44%. Clinically meaningful improvement asthma quality of life questionnaire (AQLQ) (≥ 0.5-point from baseline) was observed in the treated-group as compared to placebo (60.8% vs 47.8%, p = 0.008).

To further examine effect of omalizumab, Bousquet et al. pooled the results of five double-blind trials and two open-trials in patients with severe persistent asthma. The studies included 4,308 patients (2511 – omalizumab, 1797- control). Asthma exacerbation was reduced by 38% in the omalizumab group compared to placebo (p <0.0001). The rate of total emergency visit was reduced by 47% (p <0.0001) and hospital admissions were reduced by 52% (p = 0.041). From this pooled analysis, improvement with omalizumab was seen regardless of age, baseline FEV1, serum total IgE and dosing schedule. There was some suggestion that there was a relatively greater improvement in patients with worse lung functions. It should be noted that the response to omalizumab were generally observed at 16 weeks after initiation of the therapy and thus this is the recommended period for determining response to omalizumab.

Omalizumab has been thoroughly evaluated in children with moderate to severe asthma in two classic studies. The first study by Milgrom et al. appeared as early as in 2001. The study evaluated moderate to severe asthmatic children requiring inhaled corticosteroids, aged 6-12 years in a double-blind, placebo-controlled manner for 28 weeks (omalizumab 225 patients and placebo 109 patients). The dose of beclomethasone dipropionate (BDP) was kept stable for 16 weeks and was tapered down...
during the last 8 weeks. There was a significant decrease in asthma exacerbation episodes in the omalizumab group during the steroid reduction phase (18.2% vs 38.5%). Participants’ and investigators’ global evaluation of the effectiveness of treatment was in favor of omalizumab. No change in lung functions was observed. There was a decrease in the use of rescue medication and school absence in the omalizumab group. Most interestingly, the dose of BDP was significantly reduced in the omalizumab group (mean reduction 100% compared to 66% in placebo group).

More recently, a study by Lanier et al. evaluated omalizumab in a larger group of asthmatic children (6-12 years, omalizumab 384 patients and placebo 192 patients) who remained symptomatic during the last 4 weeks of a run-in period. The study was one-year long, including a 24-week fixed-steroid phase and a 28-week adjustable-steroid phase. Exacerbation rates were lower in the omalizumab both in the first (31%, \( P = 0.007 \)) and in the second phase (43%, \( P < 0.001 \)). The responses were further stratified according base-line FEV1 and the use of LABA. Consistency responses were observed independent of these two factors. Surprisingly, there was only a minimal reduction of steroid dose in both groups.

From these data, omalizumab appears to be equivalently effective as an add-on therapy for both adults and children with moderate to severe asthma. There was a substantial decrease in the exacerbation rates in the omalizumab group as well as a decrease in emergency medical visits. The response to omalizumab appeared to be independent of baseline lung functions and the use of LABA. Currently, omalizumab is primarily indicated and is licensed for use in several countries around the world mainly for patients age 6 years and above with moderate-to-severe asthma who are not adequately controlled with the use of ICS and LABA (GINA step 4).

**Pharmacology and dosing of omalizumab**

Absorption of omalizumab from subcutaneous injection sites occurred relatively slowly with peak levels occurring at 7-8 days and with a terminal half-life of 26 days. Omalizumab and IgE forms smaller complex trimers (containing an excess ratio of omalizumab: IgE) and hexamers (at equivalent molar levels) with IgE. These complexes are cleared slowly from circulation via FcγR through the reticuloendothelial system. Since these complexes cannot bind to IgE receptors (omalizumab occupies Cε3 site – the site for binding with FceRI and FceRII),

**Figure 3.** Steady-state (SS) free IgE against dose/baseline IgE in dosed in treated patients. From Casale et al. (30) (with permission).

no biological (allergic) activity is initiated. Among dose-ranging trials, Casale et al. clearly indicated that omalizumab needed to be given at 15-fold over the baseline IgE level in order to effectively reduce IgE levels (Figure 3). A simplified individual-tier-dosing schedule for omalizumab was developed according to weight and baseline serum IgE level (Table 1) to accommodate such finding. At this recommended dose, serum free IgE declines rapidly and reaches a nadir of < 50 ng/ml (20.8 IU/ml). At such level, clinical benefits of allergic asthma and rhinitis have been previously documented.

**Safety**

Most common adverse reactions from subcutaneous injection of omalizumab were local reactions occurring in approximately 40% of patients and with 12% being severe cutaneous reactions. Urticaria occurred in 11 out of 225 children (4.9%) randomized to receive omalizumab in a study by Berger et al. Despite omalizumab being an extensively humanized monoclonal antibody, the most serious adverse effect, i.e., anaphylaxis was initially reported in 0.2% of 57,300 patients receiving omalizumab in the company’s pivotal studies conducted between 2003 and 2006. In 2007, an Omalizumab Joint Task Force (OJTF) was formed by the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) to critically examine data on omalizumab-associated anaphylaxis. The OJTF published its first report in 2007 which indicated...
that events likely to represent anaphylaxis occurred in 35 patients with 41 episodes among 39,510 patients receiving omalizumab. This corresponded to an anaphylaxis rate of 0.09% of patients (with incidence of approximately 0.2%). 61% of these reactions occurred within 2 hours after the first 3 injections and 14% occurred within 30 minutes after the fourth or later reactions. OJTF issued a five-step recommendations including 1. obtaining informed consent, 2. delivery of anaphylaxis education, 3. availability epinephrine autoinjector, 4. pre-injection health assessment and 5. a waiting period of 30 minutes after each injection (with an extended waiting period after the first 3 injections to 2 hours).

In 2011, the OJTF published their second report examining additional 77 patients with possible anaphylaxis from the post-marketing survey by Genentech/Novartis. Using the recommendations in the first report, approximately 77% of the reactions would have been encountered in a medical facility and thus being adequately treated. There were some caveats to these reports, i.e., timing of reactions from the first 3 injections varied widely and some of symptoms could be confused with asthma exacerbations. Moreover, epinephrine autoinjectors are not widely available and thus limits the strength of recommendation. It is prudent that the waiting period should be strictly adhered to and plans for treatment of anaphylaxis should be thoroughly outlined before the initiation of treatment (e.g., the availability other means of epinephrine administration for countries where auto-injectors are not available, availability of means for assistance to patients in case of late reactions, etc.).

Other possible indications for omalizumab

As anticipated, omalizumab has been used in various conditions which have IgE-mediated causes (such as anaphylaxis and food allergy) and in those with possible IgE-mediated mechanisms (such as chronic urticaria and idiopathic anaphylaxis). Perhaps, the most interesting trial was the use of TNX-901 – another humanized anti-IgE in the treatment of peanut anaphylaxis in a double-blind, randomized placebo-controlled trial fashion. A high dose of TNX-901 (450 mg), given subcutaneously every four weeks for four doses, was found to increase the threshold (tolerated) dose of peanut challenge from 178 mg (half a peanut) to
Omalizumab in allergic diseases

Figure 4. Average birch pollens in countries in the Scandinavia with nasal symptoms of allergic rhinoconjunctivitis randomized to receive omalizumab (E25) vs placebo. From Adelroth et al. with permission.

2806 mg (nine peanuts)\textsuperscript{36}. Despite a favorable result, TNX-901 was not selected further for clinical development. Recently, a pilot, non-randomized trial of omalizumab in food-sensitive individuals, in a clinical setting was reported\textsuperscript{52}. Twenty-two adult patients sensitized to variety of foods were given omalizumab at dosage range of 150-300 mg, q 2-4 weeks. Clinical improvements in all patients were noted after 6 doses. Very recently, a collaborative, a phase II dose-finding study of omalizumab in peanut anaphylaxis was reported\textsuperscript{53}. Omalizumab was given at the same dosage for asthma as described above for 24 weeks (6 doses). In spite of a reduction of free IgE levels as a result of the treatment, only 2 of 9 patients treated with omalizumab were able to tolerate more than 1000 mg of peanut flour at the end of the treatment. From these data, it appears that the use of omalizumab in the treatment of food allergy requires further investigations and omalizumab could not be recommended for use for severe food allergy at present.

Casale et al. evaluated varying doses of omalizumab (50, 150 and 300 mg) given to allergic rhinitis patients who were sensitized to ragweed in a double-blind, placebo-controlled fashion\textsuperscript{54}. Omalizumab was given 2 weeks prior to the ragweed season and then q 3 weeks for 4 cycles. Improvements in symptoms were observed in a dose-dependent fashion, particularly in the 300 mg group. Similarly, in a large randomized study among birch-sensitive allergic rhinitis patients, Adelroth et al. demonstrated that omalizumab 300 mg given 2-3 times during birch pollen season could significantly reduced nasal symptoms and rescue medications used along with improvement in quality of life (Figure 4.)\textsuperscript{48}.

Concomitant administration of omalizumab with allergen immunotherapy has been tried in children sensitized to birch and grass pollens. Greater improvement in symptoms was observed in groups who received omalizumab in addition to allergen immunotherapy\textsuperscript{55}. Moreover, omalizumab was evaluated in combination with rush immunotherapy to ragweed (12 weeks of dual omalizumab and immunotherapy). Fewer side effects from immunotherapy were clearly observed in the omalizumab group\textsuperscript{56}. In addition, a 5-fold reduction of anaphylaxis was observed in the group receiving omalizumab comparing to those receiving immunotherapy alone. However, it is not clear how these investigations would translate into the long-term efficacy, outcome and cost-effectiveness among patients requiring allergen immunotherapy.

Omalizumab has been tried on an individual basis in patients with chronic urticaria and was found to be effective in patients with low and high baseline IgE\textsuperscript{57-60}. Recently, a double-blind, dose-determining study becomes available. Omalizumab was given as a single dose from 75-600 mg with an observation period of 4 weeks. The effect was best seen with the 300 mg dose and was apparent as early as one week\textsuperscript{61}.

Atopic dermatitis (AD) is another atopic condition for which researchers are striving to improve care. Omalizumab has been tried in AD with varying results\textsuperscript{62-64}. The reason of such discrepancies was perhaps the heterogeneity of pathogenesis and severity of disease among AD patients. Belloni et al. recently reported that at low dose of omalizumab, only 6 out of 11 patients with AD improved\textsuperscript{65}. In contrast, in a pilot study by Sheinkopf et al among 21 adults with AD, with varying baseline IgE levels (some of which were very high), omalizumab demonstrated satisfying results in all patients. Obviously, a more uniform protocol for studying omalizumab in AD is required to determine the appropriate dose and to determine which patients with AD should receive omalizumab.

Pharmacoeconomics and special considerations

The Gaining Optimal Asthma Control (GOAL) study has shown that despite optimized treatment
with fluticasone/salmeterol, 38% of patients with severe asthma remained inadequately controlled. Moreover, after a course of oral corticosteroids was added, only a further 7% became well controlled. Thus, add-on therapy such as omalizumab, would be an alternative to consider for these patients. However, the cost of omalizumab, as for other biological agents introduced for use in other chronic diseases, is considerably higher than commonly used treatments (ICS and LABA in asthma). Recently, studies of cost-effectiveness analysis of omalizumab have been published. Modern pharmacoeconomic studies employed measures such as QALY and ICER. QALY (Quality-adjusted life year) is the incremental cost per quality-adjusted life year which is widely accepted and widely used to measure of cost-effectiveness of therapy which can capture the overall effect of treatment on the patient. ICER (Incremental Cost-Effectiveness Ratio) is the term used to describe the yearly increment cost-effectiveness ratio for the drug studied. Both terms are extremely useful for healthcare policy makers when they are deciding whether to approve reimbursements of a new drug. Obviously, the decision depends heavily on the health economic structures of individual countries and willingness to pay.

Several important cost-effectiveness analyses for omalizumab have been published and were well summarized by a review by Sullivan and Turk. Apparently, QALY and ICER depend on clinical efficacy data and the inclusion/exclusion of various direct/indirect costs as well as the death rate from asthma. Using data from the INNOVATE and ETOPA studies, the ICER was calculated to be €44,910 and €26,694 respectively. These ICERs indicated that omalizumab would be cost effective if the willingness-to-pay value was approximately €60,000. Obviously, these values suggested that omalizumab is indicated for those with severe uncontrolled disease (with ICS and LABA) among whom healthcare cost is high. It is imperative that such national economic evaluations be carried out and appropriate national healthcare panels be consulted about reimbursement for omalizumab. Surprisingly, when the QALY for omalizumab was compared with those for other biological agents used for other chronic diseases (infliximab, etanercept, etc.), omalizumab compares favorably to them.

Conclusions

Omalizumab represents a culmination of the application of the findings from intensive research in allergy to clinical allergy practice (translational medicine). Biomedical engineering techniques allowed us to generate a useful molecule with a low incidence of side-effects. The clinical applicability of omalizumab in allergic diseases is potentially vast. However, due to the high cost-effectiveness ratios for this newly developed agent, omalizumab is currently indicated in only patients with moderate-to-severe asthma who have exhausted other conventional treatments for asthma. In the future, further refinement of molecules will lead us to even more improved and refined therapy for allergic diseases. Reduction in the price of omalizumab will make the drug more widely available to the public.

Acknowledgement

This review has been supported by an unrestricted educational grant from Novartis (Thailand) Limited.

References


