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The use and implementation of omalizumab as food allergy treatment: Consensus-based guidance and Work Group Report of the Adverse Reactions to Foods Committee of the American Academy of Allergy, Asthma & Immunology

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Omalizumab was recently approved by the US Food and Drug Administration for treatment of any single food allergy or multiple food allergies in children aged 1 year and older and adults. There is currently no formal guidance regarding recommended best practices for omalizumab use in food allergy, including patient selection, anticipated goals and outcomes of therapy, procedure for monitoring patients who elect to start omalizumab therapy, and ways in which omalizumab can be incorporated into the landscape of food allergy management and daily clinical practice. This work group report was developed by the food allergy therapies subcommittee of the Adverse Reactions to Foods Committee within the American Academy of Allergy, Asthma & Immunology. Consensus, evidence-based guidance regarding experts' recommendations for using omalizumab to treat children and adults with food allergy was developed by using modified Delphi methodology. In iterative fashion, a total of 8 statements regarding how to use omalizumab to treat patients with food allergy were developed

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by 16 clinical experts. This guidance provides the clinician with a suggested approach to patient selection, initiation of therapy, monitoring of efficacy, and long-term follow-up care. The role of preference-sensitive care is emphasized, with most statements offering care recommendations relevant to the culture and values of a particular practice setting. (J Allergy Clin Immunol 2025;155:62-9.)

Key words: *Omalizumab, food allergy, anaphylaxis, allergen avoidance, IgE, oral food challenge, multiple food allergies*

Abbreviations used

AAAAI: American Academy of Allergy, Asthma & Immunology
FDA: US Food and Drug Administration
OFC: Oral food challenge
OIT: Oral immunotherapy
OUtMATCH: Omalizumab as Monotherapy and as Adjunct Therapy to Multiallergen Oral Immunotherapy in Food Allergic Children and Adults
PDT: Practices, diagnostics, and therapeutics

On February 16, 2024, omalizumab (Xolair, Genentech, South San Francisco, Calif) was approved for allergen agnostic treatment of single or multiple food allergies in children aged 1 year and older and adults in conjunction with allergen avoidance.[1] Dosing follows a nomogram based on mg/kg and total IgE level, similar to but distinct from asthma dosing, on an every 2- to 4-week dosing interval, with patients receiving between 75 and 600 mg per dose. There are insufficient data to recommend dosing for food allergy for patients with a total IgE level of 30 IU/mL or less or 1850 IU/mL or more. Omalizumab therapy has no defined duration of use, does not provide long-term protection after discontinuation, and was approved to be used with ongoing allergen avoidance.[2]

Omalizumab provides a long-awaited new treatment option for interested patients and families. There is lack of clarity regarding the optimal patient for whom omalizumab is best indicated, how well this therapy works in comparison with other possible options (including avoidance), and both the long-term monitoring needs and possible outcomes of omalizumab use. Similarly, there are questions regarding who is best suited for omalizumab therapy and how this therapy can be best implemented in practice.[3-5] Omalizumab has been approved for use in asthma since 2003, and many allergists are familiar with the drug, its dosing, and its long-established safety record.[2,6] However, unlike its other indications, omalizumab's approval in food allergy is as a primary therapy, with no need for the patient to be refractory to other treatments.[1] There is a need for guidance on how this drug can be incorporated into food allergy management. Therefore, the food allergy therapies subcommittee of the Adverse Reactions to Foods Committee within the American Academy of Allergy, Asthma & Immunology (AAAAI) has developed this work group report to help provide consensus, evidence-based guidance, and experts' recommendations for using omalizumab to treat children and adults with food allergy. The aim of the guidance is to assist the practicing allergist in incorporating this new tool into treatment of patients with food allergy.

METHODS

With the approval of the Practices, Diagnostics, and Therapeutics (PDT) Committee of the AAAAI, a work group was developed from members of the Adverse Reactions to Foods Committee. This group was chosen on the basis of experience in guideline development, food allergy therapy clinical trials, and clinical practice in implementing system-level clinical practice and policy change. The work group chairs (A.A. and M.G.) performed a literature review to detail the safety and efficacy of published uses of omalizumab for food allergy and to inform, coordinate, and develop 15 initial themes for candidate good practice statements within the context of omalizumab use in food allergy. These themes encompass how patients being considered for this therapy are diagnosed with food allergy; how the underlying severity of the allergy should be considered in the context of treatment, nature of the food allergy, patient age, patient comorbidities and control of these comorbidities, and patient adherence to past treatments; consent and documentation of key outcomes that are important to follow over the long run; incorporation of home use and self-administration; determinants of success of therapy; duration of therapy; provision of support in the event of rejection of claims by payers or request for additional documentation of medical necessity; complications of therapy and management of adverse events; patient monitoring; carriage of epinephrine and risk taking; and the role of shared decision making. Between March 18, 2024, and May 16, 2024, the initial 15 themes and potential candidate statements were iteratively refined by the work group through 2 rounds of discussion, topic adjustment, and statement rewording and enhancement, during which panelists were also encouraged to submit free text comments regarding each statement. This iterative process resulted in a set of 10 statements for the first round of the modified Delphi panel. Voting for the modified Delphi panel followed a 5-point Likert scale (1 = strongly disagree; 2 = agree; 3 = neutral; 4 = agree; 5 = strongly agree). Additionally, for each candidate statement, the clinical impact method was used to rate the perceived importance of including the statement in report on a scale of 0 to 10 scale (0 = not important, 5 = neutral, 10 = very important).[7,8] The median importance score (0-10) and the corresponding range were reported for each statement. Voting was slated to continue until consensus threshold was met or for a total of 3 rounds before a statement would be categorized as "consensus not reached." Consensus was defined as agreement or disagreement equal to or exceeding 75% for themes and statements, and the minimal importance score of any statement for inclusion was set at 7 of 10. Where appropriate, statements with similar themes, achieving both consensus and clinical importance, were combined into a single statement for the final report, resulting in 8 final statements.

This study was approved by the PDT committee of the AAAAI and approved as exempt from ongoing review by the University of Cincinnati Institutional Review Board for conduct of the Delphi panel. The PDT committee provided internal review and final permission for this report to be submitted to an AAAAI journal for peer review.

RESULTS

For all the following statements, threshold agreement and minimal clinical importance was achieved for the voting on this recommendation in the first round of voting within the writing

group (see Table E1 in the Online Repository at www.jacionline.org).

Statement 1: Omalizumab is a potential treatment option that can be offered to patients with 1 or more IgE-mediated food allergies who are seeking therapy, without restriction based on disease severity or failure of alternative food allergy therapies. However, such factors may be considered as part of a shared decision-making process in considering choice of a possible therapy with the patient and family.

Discussion: On the basis of the results of the Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen Oral Immunotherapy in Food Allergic Children and Adults (OUtMATCH) study, a pivotal phase 3 trial of omalizumab as monotherapy for single– and multiple–food allergy therapy, the US Food and Drug Administration (FDA) has approved allergen agnostic use of omalizumab for treatment of 1 or more food allergies.[1,9] Although the study required that all subjects have peanut allergy plus allergy to 2 other foods (milk, egg, wheat, walnut, cashew, hazelnut), this was a pragmatic choice of allergens for purposes of a clinical trial (based on the prevalence of different food allergens) and not intended to indicate that the therapy would not work with fewer or different allergens not studied.[10] Similarly, although the trial excluded individuals with a history of severe anaphylaxis (defined as neurologic compromise or requiring intubation, for safety concerns regarding oral food challenges [OFCs]), patients with poorly controlled or severe asthma, eosinophilic gastrointestinal disorders, selected concurrent medication uses, and prior or current cancer, these exclusions were also intended for the purposes of a clinical trial and not intended to indicate that the therapy would not work in real-world settings for patients with these conditions.[9,10] Omalizumab therapy can be considered as a potential first-line treatment option for patients aged 1 year and older who have 1 or more IgE-mediated food allergies, to reduce the risk of immediate hypersensitivity reactions, in conjunction with food avoidance, consistent with the FDA approval language. This age range differs slightly from that of omalizumab's other established indications, but it is consistent with the epidemiology of food allergy being diagnosed in very young children. Additional restrictions, such as in whom or how omalizumab can be used in food allergy (eg, allergen type, degree of allergen sensitization or threshold, or with the requirement that other therapy be trialed first) that are placed above and beyond the labeling indication as approved by the FDA pose an undue burden on patients who may benefit from such therapy.[1,2]

Statement 2: All candidates for omalizumab therapy for food allergy should have (1) a qualifying total IgE level to assist with dosing along the nomogram (> 30 to <1850 IU/mL), as well as (2) evidence of sensitization determined via either (or both) a positive result of food-specific skin prick test or measurement of serum-specific IgE level to a food that would indicate a high likelihood of having an IgE-mediated reaction within the context of the patient's history. It is suggested that testing be obtained within 12 to 18 months of starting therapy.

Discussion: The FDA-approved dosing nomogram for omalizumab use in IgE-mediated food allergy is shown in Fig 1.[2] All patients who wish to initiate omalizumab therapy must have a recent total IgE level obtained within 12 to 18 months of initiation of therapy to ensure appropriate dosing. There are limited data regarding omalizumab safety and efficacy in patients with total IgE levels less than 30 IU/mL or higher than 1850 IU/mL.[11-13] As part of documenting an IgE-mediated food allergy, patients should have either skin prick testing resulting in a wheal size 3 mm or more than the negative control or a serum-specific IgE (sIgE) level greater than 0.1 kU/L or 0.35 kU/L (depending on the reporting standard of the laboratory), indicating food sensitization.[14] Obtaining both skin testing and sIgE testing is not required as long as sensitization can be documented to 1 or more foods. Measurement of either sIgE level or a skin prick testing result may become unreliable after therapy has been started.[2] Future research is needed to evaluate whether weight per IgE level–based dosing or dosing based only on weight (without considering the patient's IgE level) provides better clinical efficacy.[11]

Statement 3: OFC is not required to start omalizumab therapy. However, candidates for omalizumab or any food allergy therapy should have a clear, preferably objective, reaction history in the setting of evidence of IgE sensitization to the food. In instances in which the diagnostic history may be less certain or the allergy diagnosis is based only on sensitization without a history of symptomatic ingestion (apart from very limited contexts in which positive testing may indicate a high probability of allergy), the clinician is advised to consider the risks and benefits of performing OFC to improve the certainty of the diagnosis.

Discussion: Before initiating omalizumab or any food allergy therapy, the prescribing clinician should have high certainty that the patient has demonstrated objective symptoms of an IgE-mediated reaction to 1 or more foods, along with evidence of sensitization.[14] There are certain, very limited contexts on which sensitization in the absence of an objective history of symptomatic food ingestion may be sufficient to support a higher probability of diagnosis (Table I). However, in most other contexts (Table I), sensitization alone without a clear objective reaction history may not always indicate food allergy, and the certainty of diagnosis in such cases may be improved through OFC.[14] Please refer to the 2020 Peanut Allergy Diagnosis parameter for guidance regarding how to assess the pretest probability of the history being consistent with food allergy, and how to use diagnostic testing to convert this probability to posttest odds of a diagnosis.[14] This approach, although specific for peanut, can be used for any other food allergen. For patients who have an objective reaction history and sensitization to 1 food but are sensitized to only that food and without a history of sensitization to additional foods, the decision to offer OFC to improve the diagnostic certainty for those other foods can be approached in the context of shared decision making, given that omalizumab is also indicated for treatment of single-food allergy.

Statement 4: Determining a baseline allergen threshold for reactivity is not required to start omalizumab therapy. However, clinicians should consider performing a threshold OFC before initiating omalizumab therapy if this is a specific goal established by the patient and family as part of a shared decision-making process.

Discussion: Although in the OUtMATCH trial, multiple OFCs with entry threshold tolerance limits were part of the entry criteria, these were designed to satisfy FDA-established regulatory end points for primary efficacy and were not intended to be real-world use criteria.[9,10,15,16] Additionally, the trial data should not be interpreted as indicating that omalizumab would show benefit only in patients with qualifying thresholds similar to those in the trial. Clinicians and patients, in the setting of a shared decision-making context and based on individualized therapy goals, may wish to perform a pretherapy threshold OFC to 1 or

Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight (kg)												
		≥10-12	>12-15	>15-20	>20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90 - 125	>125 - 150
		Dose (mg)												
≥30 - 100	Every 4 Weeks	75	75	75	75	75	75	150	150	150	150	150	300	300
>100 - 200		75	75	75	150	150	150	300	300	300	300	300	450	600
>200 - 300		75	75	150	150	150	225	300	300	450	450	450	600	375
>300 - 400		150	150	150	225	225	300	450	450	450	600	600	450	525
>400 - 500		150	150	225	225	300	450	450	600	600	375	375	525	600
>500 - 600		150	150	225	300	300	450	600	600	375	450	450	600	
>600 - 700		150	150	225	300	225	450	600	375	450	450	525		
>700 - 800	Every 2 Weeks	150	150	150	225	225	300	375	450	450	525	600		
>800 - 900		150	150	150	225	225	300	375	450	525	600			
>900 - 1000		150	150	225	225	300	375	450	525	600				
>1000 - 1100		150	150	225	225	300	375	450	600					
>1100 - 1200		150	150	225	300	300	450	525	600					
>1200 - 1300		150	225	225	300	375	450	525						
>1300 - 1500		150	225	300	300	375	525	600						
>1500 - 1850			225	300	375	450	600							

Insufficient data to Recommend a Dose

*Dosing frequency:

Subcutaneous doses to be administered every 4 weeks

Subcutaneous doses to be administered every 2 weeks

FIG 1. Omalizumab dosing nomogram for IgE-mediated food allergy. *Freq,* Frequency.

more foods, but this is not required. It may not be feasible, safe, or ethical to perform or require threshold OFC(s) before starting omalizumab therapy, in particular, in those with well-documented, objective, and potentially severe past reactions (eg, requiring prior intensive care unit admission as a result of food-induced anaphylaxis).[14]

Statement 5: Clinicians should consider assessing treatment success against individualized goals that the patient and prescribing clinician have set for therapy. A shared decision-making approach is recommended. Any OFC to assess treatment response should be offered no earlier than 16 to 20 weeks after initiating omalizumab therapy. For patients with allergy to multiple foods, response should be considered as achievement of such goals for at least 1 (but not necessarily all) of the foods in question. In nonresponding patients, the clinician should strongly consider discontinuation of omalizumab given lack of benefit.

Discussion: After 16 to 20 weeks of treatment in the OUtMATCH trial, responders had to tolerate a single dose of 600 mg of peanut or 1000 mg of milk, egg, wheat, cashew, walnut, or hazelnut without dose-limiting symptoms during exit OFC. These end points were chosen to satisfy FDA-established regulatory requirements for primary efficacy in food allergy clinical trials and were not intended as real-world criteria for use.[9,10,15,16] Moreover, these end points do not represent the only potentially meaningful or protective doses of allergen to represent treatment response.[17,18] It is of note that 33% of patients randomized to the active treatment in OUtMATCH did not show treatment response (as defined by the trial) when it was assessed between 16 and 20 weeks of therapy. However, in the open label extension phase, with additional treatment time among a sample of 60 subjects, an additional 34% improved their allergen threshold, whereas 45% had no additional gain and 21% lost some threshold (primarily for peanut) when assessed after 40 to 44 weeks of therapy.[9]

Clinicians are encouraged to discuss potential goals of therapy with patients, as well as plans for assessment of response to therapy in advance of starting omalizumab therapy, as part of a shared decision-making context.[18,19] Patients should be made aware of the primary efficacy data but also encouraged to pursue individualized goals that matter to them. Examples of such possible goals among various potential considerations may include an interval history of tolerated accidental ingestions, improvements in quality of life, or discreet changes in allergen threshold.[17] Clinicians who wish to perform any OFC to verify potential change in threshold should strongly consider waiting a minimum of 16 to 20 weeks after initiating therapy before

TABLE 1. Guidance for determining if an OFC can enhance diagnostic certainty

Probability of IgE-mediated food allergy	Scenario	Likelihood of changing diagnostic certainty
High	● Documented failed OFC due to clear objective symptoms. ● Documented history of a reaction attributable to a specific single food allergen with objective symptoms. Reaction is not attributable to irritation from skin contact and did not occur in the setting of a concurrent viral/bacterial infection. Patient is sensitized to this food.	**Unlikely**
Moderate	● Documented failed OFC due to subjective symptoms. ● Documented history of a reaction attributable to one or more potential food allergens, but unclear which, with objective symptoms. Reaction is not attributable to irritation from skin contact and did not occur in the setting of a concurrent viral/bacterial infection. Patient sensitized to one or more of these foods. ● Immediate, objective flaring of eczema, which had been dormant during at least 2 weeks of single food allergen removal, with no other treatments used to manage the eczema, in a patient sensitized to that food.	**Possible**
Low	● Documented history of a reaction attributable to a known food allergen or allergens, with objective or subjective symptoms developing, but occurring in the setting of a concurrent viral/bacterial infection. Patient is sensitized to the food/foods. ● Patient given the diagnosis of a food allergy (or allergies) based on skin or blood testing done in the setting of eczema as an infant/toddler without having ingested the food. ● Testing done for the purposes of food allergy screening or to assess cross-reactivity in the setting of a primary allergy to one food item where the cross-reactive foods have not been ingested. ● Documented history of a subjective or contact reaction possibly attributable to one or more possible food allergen or allergens, but it is unclear specifically to which food allergen, and occurred in a patient with sensitization to this/these food/foods. ● Documented history of a reaction attributable to a known food allergen or allergens, with objective or subjective symptoms developing that occurred from ingestion and distinct from or occurring in the setting of a concurrent viral/bacterial infection. ● Symptoms occurred at least 3 hours or longer after ingestion and were not related to pork/meat ingestion in someone with possible history of lone star tick bite.	**Probable**
Very Low	● Only evidence of allergy is sensitization to food/foods obtained without a relevant history of an objective reaction. ● Positive non-IgE testing or other unapproved testing methods to food or foods. ● Any sensitization in a person with a history of having eaten the food(s) in question without developing symptoms. ● Any sensitization in a person with symptoms developing >6 hours after ingestion, unrelated to pork/meat ingestion in someone with possible history of lone star tick bite. ● Only evidence of food allergy is development of non-bothersome urticaria or perioral/facial rash or other rash in an area where the food made skin contact but the patient is sensitized to the food. ● Only evidence of food allergy is any type of cutaneous symptoms that repeatedly occur over hours or days despite antihistamine or epinephrine treatment, but the patient is sensitized to the food. ● Reaction cannot be clearly distinguished from toxic or other metabolic process in a patient sensitized to the food.	**Likely**

offering an OFC (consistent with the timing of assessment in OUtMATCH, which was guided by company data regarding the timing of when a response could reasonably be expected).[9] If after an initial assessment for benefit there is not a clinical response (in particular, if this assessment occurs closer to the aforementioned minimum course of therapy), clinicians may consider continuing therapy for an additional period of time before reassessment for benefit, as some patients may respond with longer duration of therapy. For patients who do not respond to therapy according to their desired goals, there should be a discussion to consider discontinuing therapy given lack of benefit. For patients being treated for multiple food allergies, response should be gauged on the basis achieving a goal for at least 1, but not necessarily, all foods.

Statement 6: Omalizumab is approved for treatment in conjunction with strict food allergen avoidance and not in combination with oral immunotherapy (OIT) or permissive allergen ingestion. Clinicians who offer off-label uses of omalizumab should document this discussion with patients, including any protocols, parameters, or safe-dosing rules.

Discussion: The FDA has approved omalizumab use in the treatment of single or multiple food allergies across a broad age range, without specifying which particular allergens. This approval was granted with a caveat that use is intended to be in conjunction with allergen avoidance and epinephrine carriage to provide protection against reactions in response to accidental ingestions.[1,2]

Stage 2 of OUtMATCH had yet to be published at the time when these statements were finalized, but they will study the use of omalizumab facilitation during the buildup phase of multifood OIT.[10] Multiple other small studies have shown that omalizumab-facilitated OIT buildup enables a faster progression through this stage, with lower rates of adverse events than with OIT buildup without omalizumab.[11,20-36] However, these data have also shown that once omalizumab is withdrawn, many patients may develop adverse events while continuing OIT (including some that prompt resumption of omalizumab therapy).[11,23,25,27,28,31,33,35]

Combining omalizumab with OIT has not been shown to improve the likelihood of developing sustained unresponsiveness versus with OIT alone.[26] Similarly, several small studies have noted that patients undergoing sustained omalizumab treatment have had variable increases in their allergen threshold (across multiple foods), allowing for regular, periodic open consumption of such foods without reaction.[21,37,38] This particular outcome is not being studied in OUtMATCH.[10] Recent meta-analysis has affirmed the aforementioned benefits and safety of both combined use with OIT and the open individualized threshold–guided consumption of allergen while undergoing omalizumab therapy.[21]

Although such data are encouraging, these applications remain outside the FDA-approved label, have not undergone rigorous study as part of a registration trial, and as such are considered off-label applications. The AAAAI makes no comment as to off-label use. However, the AAAAI recognizes that, in their capacity as autonomously practicing clinicians, many clinicians may engage in off-label practices at their own risk. The authors of this document would advise any clinician who elects to engage in any off-label practices that this be done in the setting of a shared decision-making discussion with the patient and that the clinician strongly consider both obtaining informed consent and documenting whatever protocol or practice style is recommended to the patient in the chart.

Statement 7: There are no contraindications to concurrent administration of inactive or live vaccination while on omalizumab treatment.

Discussion: There is no concern that omalizumab would interfere with vaccine efficacy or pose a safety risk to receiving any type of vaccine. Omalizumab's mechanism of action is unrelated to the formation of IgG or IgA vaccine titer from plasma cells or their activity, or development of T-cell–mediated immunity.[39,40] Because historically omalizumab was not indicated in individuals younger than 12 years, no formal study of vaccine safety with live or inactivated agents has been conducted.[2] Because use in food allergy is indicated in individuals as young as 1 year, it may overlap with recommended concurrent administration of both live and inactivated vaccines. However, despite the lack of formal study, there is no theoretic or clinical concern that omalizumab use would impair development of immunity after vaccination or increase the risk of viral dissemination after live vaccination. Clinicians should encourage their patients to receive all regularly scheduled vaccines while taking omalizumab, as they would for their patients not taking omalizumab.

Statement 8: Prior to initiation of omalizumab therapy, we recommend discussion with families and patients regarding their comfort for home dosing. The clinician is encouraged to create a plan to assist patients in gaining comfort with and to support the transition to home use, as well as to facilitate dosing compliance. Consider regularly scheduled interim nursing or clinician calls, electronic messaging, telehealth visits (including visits to observe home dosing), or office visits to help foster injection adherence to the home dosing phase, monitor for any emerging issues, and provide routine food allergy follow-up.

Discussion: In the United States before 2020, omalizumab was not available in the prefilled syringe or the new autoinjector, meaning that doses needed prolonged preparation time for reconstitution from a vial and were able to be administered only in a medical office.[2] With the availability of the prefilled syringe and now the autoinjector forms, the FDA allows for home administration after the third dose (because of a 0.2% rate of anaphylaxis, the first 3 doses should be administered in the office).[2] Data have shown that home use after 3 observed doses is more cost-effective than dosing under observation in the office, and home dosing is the preferred long-term option for administration.[41] More recent data as part of an overall cost-effectiveness evaluation of omalizumab use in food allergy suggest that no required in-office dosing is the most cost-effective strategy.[42]

Before therapy is started, it is important to assess the patient (and his or her guardians, where applicable) for ability and readiness to adhere to the home dosing requirements. Some patients may require additional teaching on administration, potential pain management, and coaching to be ready to transition to home dosing. Secure messaging through electronic medical records, telehealth visits, or even in-person office visits should be considered to help monitor adherence, troubleshoot any issues, and provide encouragement. Clinicians are advised that skin and sIgE testing will become unreliable markers of food sensitization to follow after omalizumab therapy has been started.[2] However, patients still require interim in-person visits for routine follow-up at least annually, as well as for renewal of epinephrine autoinjector prescriptions, updating of their allergy action plans, and renewal of omalizumab prescription.

Additional considerations

Concurrent management of atopic comorbidities. For patients with food allergy and specific atopic comorbidities for which omalizumab is also indicated (asthma, chronic rhinosinusitis with nasal polyps, chronic urticaria), omalizumab dosing initiated for food allergy may provide better control of these comorbidities and allow for other nonbiologic medication reduction to potentially consolidate therapy.[2] A shared decision-making approach is recommended when considering any medication consolidation. Clinicians should consult current clinical practice guidelines when considering adjusting concomitant medication use for other atopic comorbidities.

Approach to shared decision making. Initiating omalizumab or any food allergy therapy is preference sensitive; it is an option for a patient and/or family to consider—not a necessity. With the growing number of options for food allergy therapy, shared decision making is even more crucial. Unlike omalizumab's use in urticaria, nasal polyps, or asthma, in food allergy it can be used as a first-line therapy and patients do not need to demonstrate progressive failure of other strategies to qualify for use. Most patients and families would likely benefit from undergoing a detailed discussion to ensure that they understand their management options and are fully informed regarding the risks, benefits, obligations, and commitments of each therapy option.[18,19]

Payer issues. Despite the fact that omalizumab is approved as a first-line option without any disease severity qualification or requirement that some other therapy has failed, clinicians should expect that certain payers may implement eligibility criteria not specified by the FDA in its approval or require both a letter of medical necessity and appeal before approving omalizumab for food allergy.[1,2] This work group report strongly encourages payers to follow the guidance specified in this document as a pragmatic and evidence-based approach to patient selection for omalizumab therapy. Furthermore, this work group discourages payer *ad hoc* establishment of additional restrictions or eligibility criteria that supersede those specified in the product label as approved by the FDA, given that this unnecessarily restricts

patients' access to potentially beneficial therapy indicated for their disease state.

DISCUSSION

This document outlines consensus-based guidance for the approach to use and implementation of omalizumab for the treatment of IgE-mediated food allergy. This pragmatic document provides the clinician with a suggested approach to patient selection, initiation of therapy, monitoring of efficacy, and long-term follow-up care. This guidance recognizes the preference-sensitive nature of therapy for food allergy when multiple treatment options exist and emphasizes shared decision making, individualization, and consideration for patient values and preferences with every step. As such, this work group report remains guidance, and most of its statements offer suggestions for care that operates within the culture and values of a particular practice setting, with few instances of more emphatic recommendations for a particular action. As more data regarding potential additional applications of omalizumab for treating IgE-mediated food allergy emerge, this guidance will likely evolve through focused update. This will likely include real-world use data from centers that have monitored their processes and outcomes, to help inform best current practices.

As noted within these recommendations, there are distinct differences between the planning, operation, and outcomes of large randomized controlled clinical trials for product registration and the more pragmatic, real-world approaches that shape the daily practice environment.[43] Thus, few clinical trials are designed for establishing rigid inclusion or exclusion criteria as well as outcome assessment to be directly replicated and applied in real-world clinical practice. All stakeholders, including patients, advocates, clinicians, manufacturers, and payers, must recognize the rigid structure within which a registration trial that must exist, and they must be cautious about dogmatically adapting particular specific features of these trials to clinical practice as the only way in which the concept can be safely and effectively implemented. This document serves to promote a practical balance in implementing clinical trial results into practice.

This work group report has multiple limitations. First, the guidance is based largely on findings of a single, large randomized controlled trial that formed the basis for the FDA's approval of omalizumab for food allergy. Additional data regarding efficacy and safety from use in the OUtMATCH trial, as well as from real-world applications, are anticipated to help the evolution of these recommendations.[9] Second, for efficiency, a smaller core of authors helped develop the initial statements and iteratively revise them through Delphi panel consensus. Allowing all members of the Adverse Reactions to Foods Committee who indicated interest in this project to be a part of the initial development stage was not feasible. Third, this document represents an endorsed, approved AAAAI work group report, but it is not a formal policy guideline or practice parameter.

In conclusion, this document outlines consensus-based guidance for the clinician to help guide the approach to use and implementation of omalizumab for the treatment of IgE-mediated food allergy. These 8 statements will be updated periodically as additional data or practice trends evolve.

DISCLOSURE STATEMENT

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Greenhawt is a consultant for Aquestive; is a member of physician/medical advisory boards for DBV Technologies, Takeda, Griffols, Nutricia, Novartis, Aquestive, Allergy Therapeutics, AstraZeneca, ALK-Abelló, Bryn, Genentech, and Prota; is a speaker for Genentech; is an unpaid member of the scientific advisory council for the National Peanut Board and medical advisory board of the International Food Protein–Induced Enterocolitis Syndrome Association; is a member of the Brighton Collaboration Criteria Vaccine Anaphylaxis 2.0 working group; is the senior associate editor for the *Annals of Allergy, Asthma, and Immunology*; and is member of the Joint Taskforce on Allergy Practice Parameters. In addition, J. Wang has received honoraria for lectures from ImSci, Red Nucleus, Medscape, Paradigm Medical Communications, Kaplan, Food Allergy Research and Education, and multiple state and local allergy societies. The rest of the authors declare that they have no relevant conflicts of interest.

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TABLE E1. Modified Delphi voting results[a]

Statement	Agreement[b]	Importance[c]
Statement 1: Omalizumab is a potential treatment option which can be offered to patients with one or more IgE-mediated food allergies seeking therapy, without restriction based on disease severity or failure of alternative food allergy therapies. However, such factors may be considered as part of a shared decision-making process in considering choice of possible therapy with the patient and family.	4.8 (SD = 0.39)	9.3 (SD = 0.62)
Statement 2: All candidates for omalizumab therapy for food allergy should have (1) qualifying total IgE level to assist with dosing along the nomogram (> 30 to <1850 IU/mL), as well as (2) evidence of sensitization via either (or both) food-specific skin prick test or serum-specific IgE to a food that would indicate a high likelihood of having an IgE-mediated reaction within the context of the patient's history. It is suggested that testing be obtained within 12-18 months of starting therapy.	4.6 (SD = 0.49)	8.7 (SD = 0.79)
Statement 3: Oral food challenge (OFC) is not required to start omalizumab. However, candidates for omalizumab or any food allergy therapy should have a clear, preferably objective reaction history in the setting of evidence of IgE sensitization to the food. In instances where the diagnostic history may be less certain, or the allergy diagnosis is based only on sensitization without a history of symptomatic ingestion (apart from very limited contexts where positive testing may indicate a high probability of allergy), the clinician is advised to consider the risks and benefits of performing OFC to improve the certainty of the diagnosis.	4 (SD = 1.29)	8 (SD = 1.82)
Statement 4: Determining a baseline allergen threshold for reactivity is not required to start omalizumab. However, clinicians should consider performing a threshold OFC before initiating omalizumab therapy if this is a specific goal established by the patient and family, as part of a shared decision-making process.	4.3 (SD = 0.65)	7 (SD = 02.12)
Statement 5: Clinicians should consider assessing treatment success against individualized goals that the patient and prescribing clinician have set for therapy. A shared decision-making approach is recommended. Any OFC to assess treatment response should be offered no earlier than 16-20 weeks after initiating omalizumab therapy. For multi-food allergic patients, response should be considered as achieving such goals for at least one (but not necessarily all) of the foods in question. In non-responding patients, the clinician should strongly consider discontinuation of omalizumab given lack of benefit.	4.5 (SD = 0.67)	7.9 (SD = 1.78)
Statement 6: Omalizumab is approved for treatment in conjunction with strict food allergen avoidance, and not in combination with oral immunotherapy (OIT) or permissive allergen ingestion. Clinicians who offer off-label uses of omalizumab should document this discussion with patients, including any protocols, parameters, or safe-dosing rules.	4.5 (SD = 0.52)	8.3 (SD = 1.15)
Statement 7: There are no contraindications to concurrent administration of inactive or live vaccination while on omalizumab treatment.	4.6 (SD = 0.67)	7.8 (SD = 1.71)
Statement 8: Prior to initiating omalizumab therapy, we recommend discussion with families and patients regarding their comfort for home dosing. The clinician is encouraged to create a plan to assist patients in gaining comfort with and to support the transition to home use, as well as facilitate dosing compliance. Consider regularly scheduled interim nursing or clinician calls, electronic messaging, telehealth visits (including visits to observe home dosing), or office visits to help foster injection adherence with the home dosing phase, monitor for any emerging issues, and provide routine food allergy follow-up.	4.4 (SD = 0.51)	8.1 (SD = 1.31)

[a]Consensus was reached in a single round of voting.
[b]Agreement was rated on a scale from 1 (strongly disagree) to 5 (strongly agree).
[c]Importance was rated on a scale from 1(not important) to 10 (very important).