Safety of Biologics in Food Allergy: What Our Patients Need to Know

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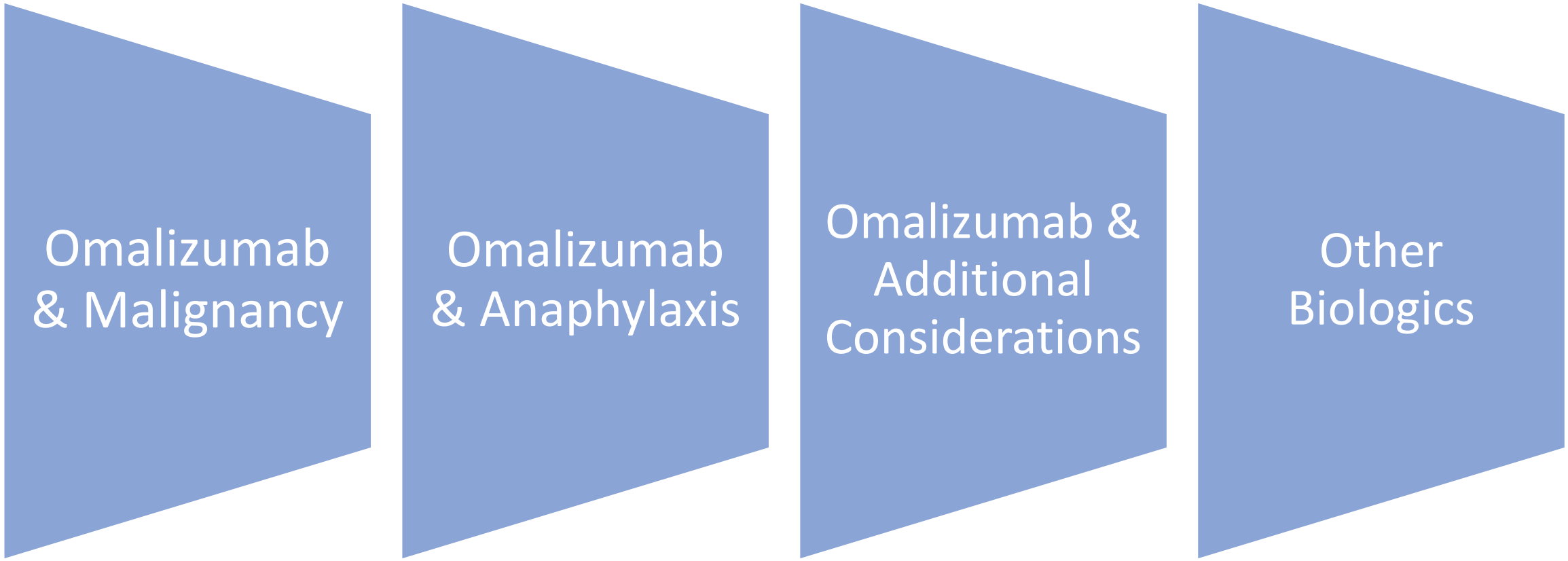
Overview



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Learning Objectives

1. Upon completion of this learning activity, participants should be able to discuss concerns about malignancy and omalizumab.

2. Upon completion of this learning activity, participants should be able to discuss concerns about anaphylaxis and omalizumab.

3. Upon completion of this learning activity, participants should be able to discuss safety profiles of biologics being studied for IgE mediated food allergy.

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Omalizumab & Malignancy

Pooled Clinical Data from Phase 1-3 Studies				
Malignancy in 20/4127 (0.5%) of omalizumab treated subjects	Malignancy in 5/2236 (0.2%) of control subjects	Wide spectrum of malignancies	4 cases of malignancy likely preceded omalizumab	Majority of patients treated with omalizumab for < 1 year

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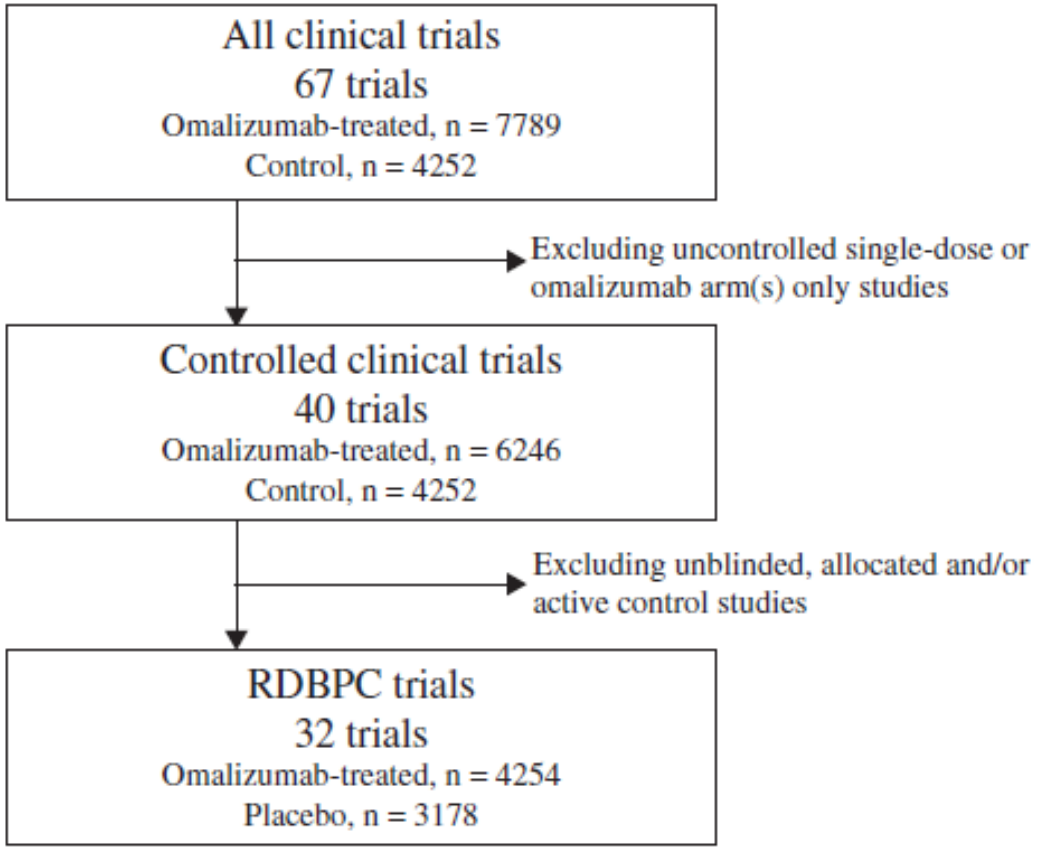
Additional Pooled Analysis



	Omalizumab (n = 4254)	Placebo (n = 3178)	Omalizumab vs placebo: Difference in rates	Omalizumab vs placebo: Rate ratio
No. of patients with primary malignancy	14	11		
Observation time (y)	3382.40	2473.79		
Incidence rate*	4.14	4.45	−0.31	0.93
95% CI	2.26 to 6.94	2.22 to 7.94	−4.47 to 3.35	0.39 to 2.27

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Busse et al. JACI 2012; 129: 983.

Prospective, Observational Cohort (EXCELS)

TABLE II. Study-emergent primary malignancy AE crude rates in enrolled patients

	Omalizumab cohort (n = 5007)	Nonomalizumab* cohort (n = 2829)	Crude differences in rates (95% CI)	Crude ratio of rates
Person-years at risk for any malignancy	18,425.5	9,962.6		
No. of malignancy events† (any type)	295	190		
Malignancy rate‡ (any type [95% CI])	16.0 (14.2 to 17.9)	19.1 (16.5 to 22.0)	−3.06 (−9.19 to 2.03)	0.84 (0.62 to 1.13)
No. of malignancies† (excluding NMSC events)	114	63		
Malignancy rate‡ (excluding NMSC [95% CI])	6.2 (5.1 to 7.4)	6.3 (4.9 to 8.1)	−0.14 (−2.23 to 1.80)	0.98 (0.71 to 1.36)

	Omalizumab cohort (n = 5007)				Nonomalizumab cohort (n = 2829)			
	No. of malignancy events				No. of malignancy events			
Tumor type	Observed	Expected	SMR	95% CI	Observed	Expected	SMR	95% CI
All malignancies (excluding NMSC)	114	125.4	0.91	0.75-1.09	63	76.8	0.82	0.64-1.04
Breast cancer	29	25.4	1.14	0.78-1.62	13	15.5	0.84	0.47-1.39
Prostate cancer	17	16.0	1.06	0.64-1.66	5	9.2	0.54	0.21-1.19
Colorectal cancer	14	11.5	1.21	0.70-1.98	3	7.2	0.41	0.11-1.11
Melanoma	8	5.4	1.47	0.69-2.78	5	3.2	1.58	0.60-3.46
Lung cancer	6	16.1	0.37	0.15-0.77	7	10.5	0.66	0.30-1.31
Thyroid cancer	7	3.7	1.91	0.85-3.76	1	2.0	0.49	0.04-2.30

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Long et al. JACI 2014; 134: 560.

Omalizumab & Anaphylaxis

Pre-marketing clinical trials	3 of 3,507 (0.1%)
Post-marketing reports (2003-2006)	114 of 57,300 (0.2%)

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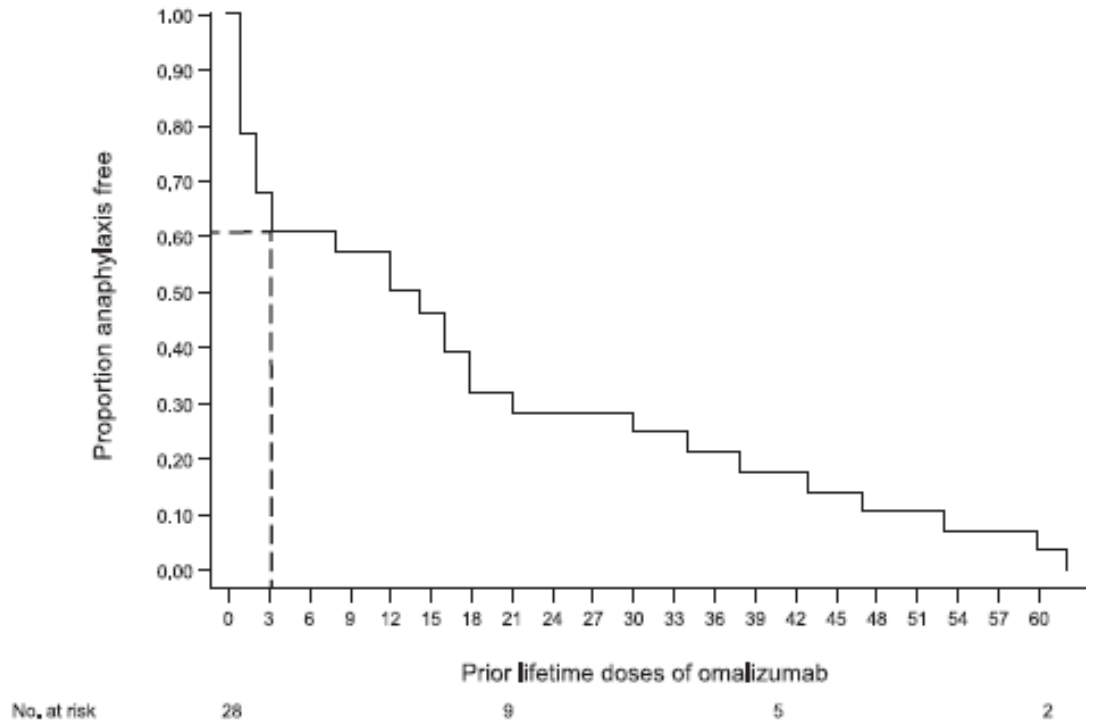
Risk Factors for Anaphylaxis

TABLE I. Demographic and baseline characteristics

Characteristic	Cases of anaphylaxis (n = 30)	Controls (n = 88)
Mean ± SD age at time of event (y)*	42.7 ± 16.4	45.4 ± 15.4
Sex: female, n (%)	27 (90.0)	60 (68.2)
Mean ± SD preomalizumab IgE (IU/mL)†	317.9 ± 416.0	455.5 ± 758.5
Mean ± SD best FEV_1 (%)‡	79.3 ± 15.9	82.9 ± 15.9
History of anaphylaxis or anaphylactoid episode, n (%)	17 (56.7)	20 (22.7)
Mean ± SD age at asthma diagnosis (y)	23.7 ± 19.5	20.2 ± 17.4
Omalizumab frequency, n (%)		
Every 2 wk	16 (53.3)	40 (45.5)
Every 4 wk	13 (43.3)	40 (45.5)
Mean ± SD total no. of omalizumab doses§	18.6 ± 19.6	58.5 ± 59.7
History of allergies/allergic rhinitis, n (%)	29 (96.7)	86 (97.7)
History of food allergies, n (%)	18 (60.0)	33 (37.5)
History of allergic reaction following any injection, n (%)	10 (33.3)	18 (20.5)



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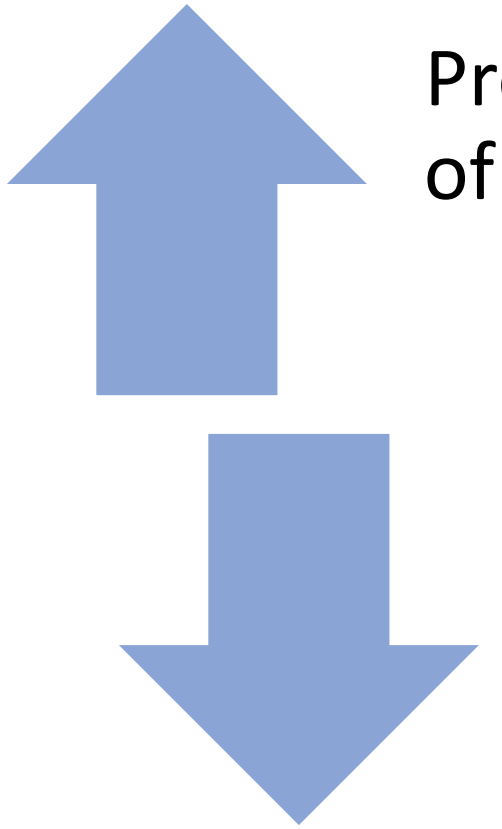
Lieberman et al. JACI 2016; 138(3): 913.

Considerations for Anaphylaxis

- 24 (80%) cases involved cutaneous, subcutaneous, mucosal or respiratory symptoms
- 21 (70%) cases treated with epinephrine
- 12 (40%) considered life threatening, 6 (20%) required hospitalization
- 0 cases of death or long term sequelae



Previous history of anaphylaxis – 0.62%

No history of anaphylaxis – 0.08%

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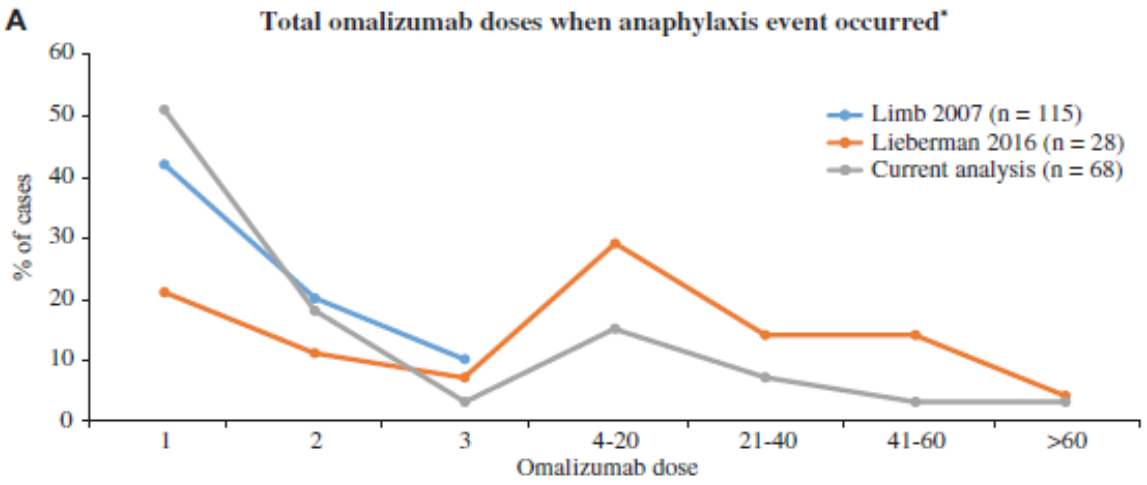
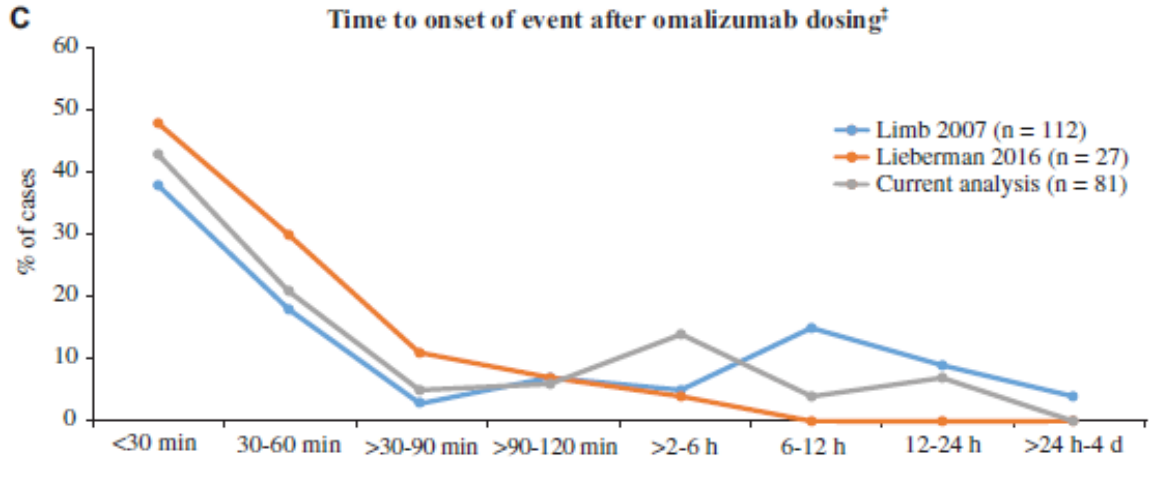
Lieberman et al. JACI 2016; 138(3): 913.

Anaphylaxis





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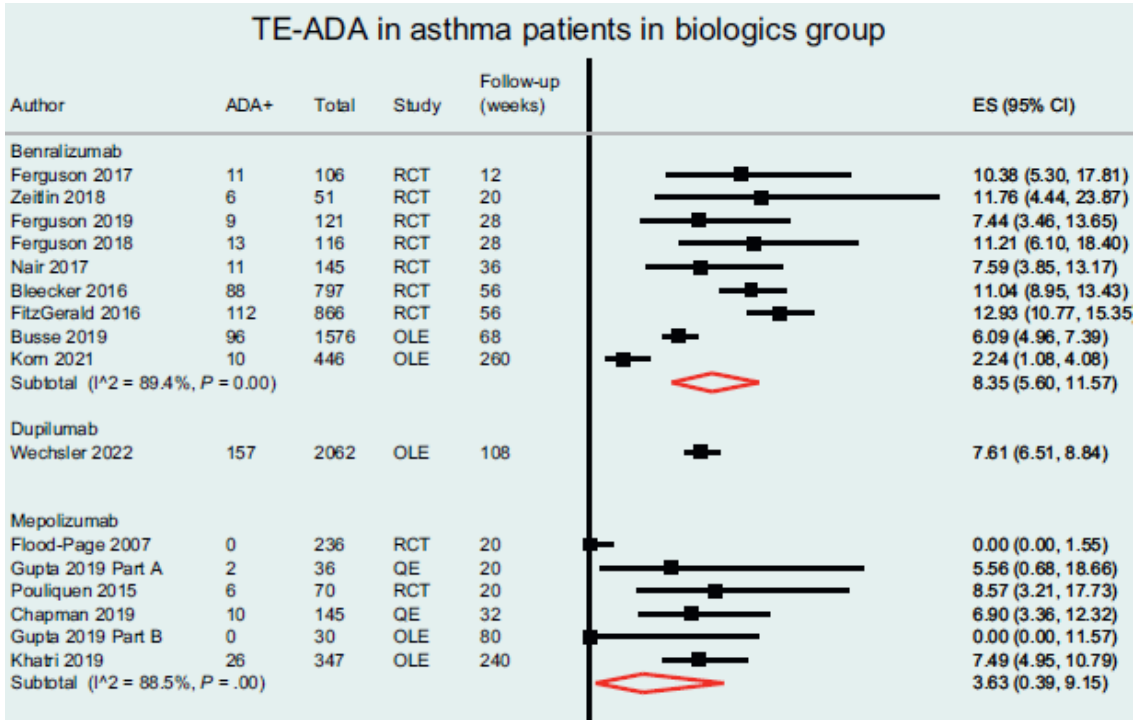
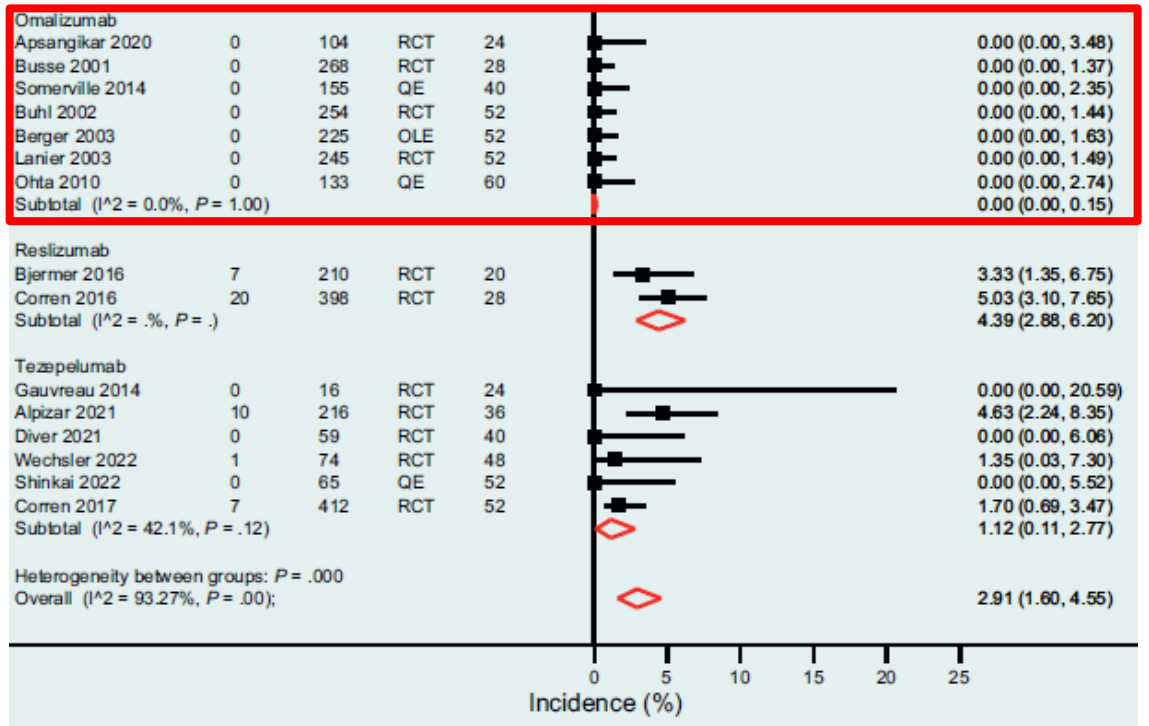
Lieberman et al. JACI 2017; 140(6): 1734.

Anti Drug Antibodies





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Chen et al. JACI IP 2023; 11: 1475.

Guidelines

The OJTF recommends that patients be kept under observation for 30 minutes after each injection. This time should be extended for 2 hours for the first 3 injections based on the data reviewed by the OJTF, as well as suggested in the 2007 National Heart, Lung, and Blood Institute Expert Panel Report 3 "Guidelines for the diagnosis and management of asthma."[3] However, this could be modified based on a physician's clinical judgment after discussing risks with the patient.

BOX 7 Recommendations for managing anaphylaxis under omalizumab treatment for CSU

The occurrence of anaphylaxis following treatment with omalizumab in CSU is an event of special interest that should be reported appropriately in order to improve the post-marketing surveillance data	Conditional recommendation, expert opinion based
The first 3 doses should be administered in a setting with experience in managing anaphylaxis; an observation period of 30 min post-administration is recommended. Thereafter, post-administration observation is at the discretion of the healthcare provider	Conditional recommendation, expert opinion based
Consultation with an allergist is encouraged if risk factors for anaphylaxis are present	Conditional recommendation, expert opinion based
As most cases are mild/moderate and respond well to anaphylaxis treatment omalizumab should not be discontinued (shared decision between clinician and patient)	Conditional recommendation, expert opinion based
Home administration is an option starting with the 4th dose with the condition that the patient has been provided with an anaphylaxis action plan and proper education	Conditional recommendation, expert opinion based

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Cox et al. JACI 2007; 120: 1373., Agache et al. Allergy 2022; 77: 17.

Guidelines

AMERICAN ACADEMY OF PEDIATRICS

Committee on Nutrition

nursing. Solid foods should not be introduced into the diet of high-risk infants until 6 months of age, with dairy products delayed until 1 year, eggs until 2 years, and peanuts, nuts, and fish until 3 years of age.

Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected

Interim guidance
13 March 2020

World Health Organization

Do not routinely give systemic corticosteroids for treatment of viral pneumonia outside clinical trials.

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Omalizumab At Home Dosing

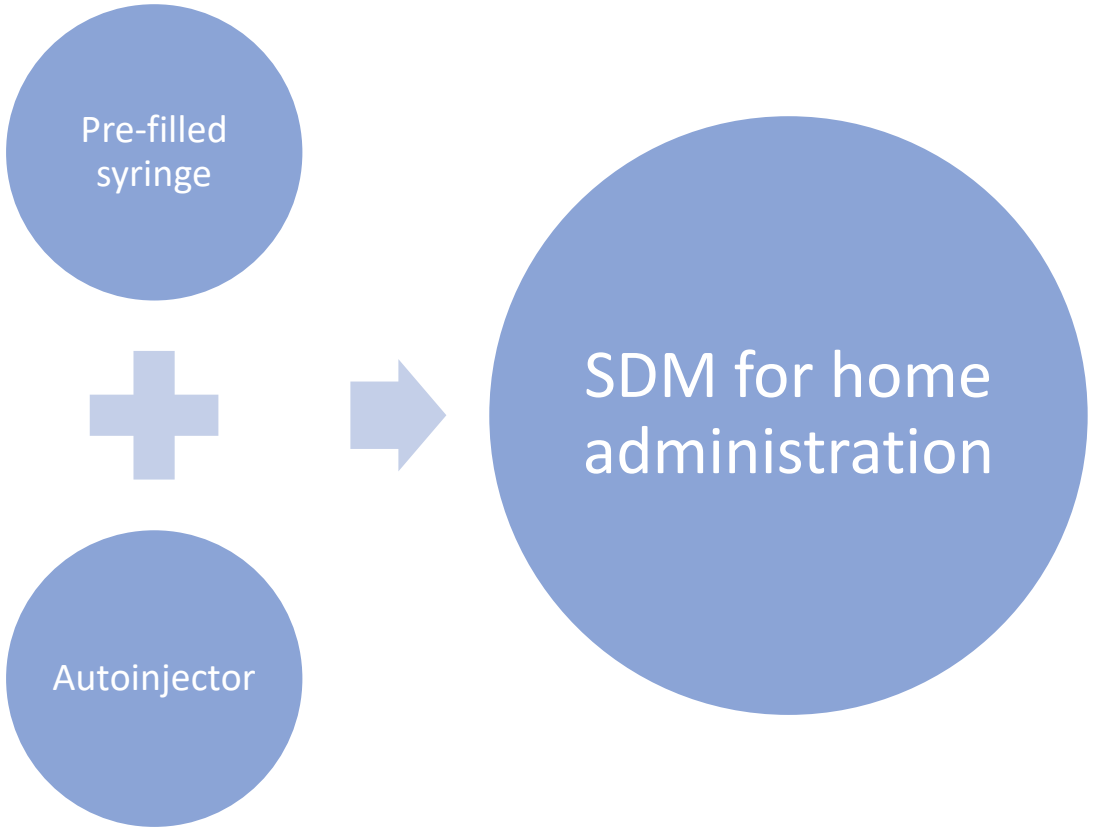
AAAAI Work Group Report

American Academy of Allergy Asthma & Immunology

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

Check for updates

Aikaterini Anagnostou, MD, PhD,[a] J. Andrew Bird, MD,[b] Sharon Chinthrajah, MD,[c] Timothy E. Dribin, MD,[d] David M. Fleischer, MD,[e] Edwin Kim, MD,[f] Anna Nowak-Wegrzyn, MD, PhD,[g] Rima Rachid, MD,[h] Marcus S. Shaker, MD, MS,[i,j] Wayne Shreffler, MD, PhD,[k] Scott Sicherer, MD,[l] Jonathan Tam, MD,[m] Brian P. Vickery, MD,[n] Yamini V. Virkud, MD, MA, MPH,[f] Julie Wang, MD,[l] Michael Young, MD,[h] and Matthew Greenhawt, MD, MBA, MSc[e] *Houston and Dallas, Tex; Palo Alto and Los Angeles, Calif; Cincinnati, Ohio; Aurora, Colo; Chapel Hill, NC; New York, NY; Boston, Mass; Lebanon and Hanover, NH; and Atlanta, Ga*



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Anagnostou et al. JACI 2025; 155: 62.

EXPECT Pregnancy Registry

Omalizumab exposure during pregnancy	Total (n = 230)
Exposure duration (mo)	
No.	230
Median (range)	8.8 (1.0-9.9)
Dose level†	
No.	216
150 mg	40 (18.5%)
225 mg	30 (13.9%)
300 mg	80 (37.0%)
375 mg	47 (21.8%)
Other	19 (8.8%)
Dosing interval (week)†	
No.	216
Every 2 wk	114 (52.8%)
Every 4 wk	97 (44.9%)
Other	5 (2.3%)
Earliest exposure	
No.	230
First trimester‡	226 (98.3%)
Second trimester	4 (1.7%)
Third trimester	0 (0.0%)
Overall exposure	
Any first trimester‡	226 (98.3%)
Any second trimester	199 (86.5%)
Any third trimester	197 (85.7%)
All trimesters	191 (83.0%)

	EXPECT subcohort* (n = 230)	QECC (n = 1153)
Age (y)		
Median (range)	30.0 (16-45)†	27.7 (15.3-44.6)‡
% <35 y	74.8%†	85.7%‡
Obesity	46.7%§	NA‖
Smoking	7.4%	NA‖
Asthma medications during pregnancy		
ICSs	81.3%	100.0%¶
Leukotriene receptor antagonists	49.6%	7.8%
Oral corticosteroids	23.7%	22.8%

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Namazy et al. JACI 2020; 145: 528.

Women of Child Bearing Age

TABLE IV. Pregnancy and infant outcomes (excluding congenital anomalies) in the EXPECT subcohort and the QECC

	EXPECT subcohort*	QECC†
Pregnancy outcomes	n = 230	n = 1153
Live births (% of pregnancies [95% CI])	99.1% (96.9% to 99.9%)	99.3% (92.9% to 100.0%)†
Fetal death/stillbirths‡ (% of pregnancies [95% CI])	0.9% (0.1% to 3.1%)	0.9% (0.3% to 1.5%)†
Live-born infant outcomes§	n = 233	n = 1162
Birth weight (kg), mean ± SD‖		
All infants	3.2 ± 0.6	3.2 ± 0.6
Singletons	3.2 ± 0.6	3.2 ± 0.3
Twins	2.4 ± 0.4	2.0 ± 0.3
Low birth weight (% of infants [95% CI])‖¶		
All infants	13.7% (9.5% to 18.9%)	9.8% (7.9% to 11.8%)
All singletons, including premature births	11.6% (7.6% to 16.6%)	8.3% (6.5% to 10.2%)
All full-term infants	4.7% (2.2% to 8.8%)	2.9% (1.8% to 4.0%)
Full-term singletons	2.7% (0.9% to 6.1%)	2.9% (1.8% to 4.0%)
Oral corticosteroid use#		
Yes	18.2% (9.1% to 30.9%)	13.7% (8.8% to 18.6%)
No	12.3% (7.8% to 18.2%)	8.7% (6.6% to 10.8%)
SGA (% of infants [95% CI])**	9.7% (6.2% to 14.4%)	15.8% (13.3% to 18.4%)
Gestational age (wk), median (range)	39.0 (28.3 to 43.0)	39.0 (20.0 to 42.0)
Premature birth (% of infants [95% CI])††	15.0% (10.7% to 20.3%)	11.3% (9.2% to 13.5%)
Oral corticosteroid use		
Yes	32.7% (20.7% to 46.7%)	16.2% (10.9% to 21.4%)
No	9.6% (5.7% to 14.9%)	9.8% (7.5% to 12.1%)

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Namazy et al. JACI 2020; 145: 528.

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

Original Article

A systematic review and expert Delphi Consensus recommendation on the use of vaccines in patients receiving dupilumab: A position paper of the American College of Allergy, Asthma and Immunology

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Anagnostou et al. JACI 2025; 155: 62., Lieberman et al. Ann All Asth Immunol 2025; 133(3): 286.

Statement	% Agree (n)	% Disagree (n)	Free-text comments
1. It is safe to administer live vaccines to patients receiving dupilumab.	89.3 (25)	0 (0)	• Very limit data • Not all live vaccines are equal. Not all patients with eczema treated with dupilumab have atopic dermatitis. • There is no immunologic basis to suggest this would be unsafe. • I think the issue is the concern for lack of response, not danger of receiving the vaccine • Small numbers of patients but data are reassuring in both children and adults • There are no convincing data of harm or decreased response to vaccination while on dupilumab • Literature on this subject is scant, as is reported clinical evidence and outcomes . . . hence the rationale for this Delphi study. However, the literature presently available is from 2020-2022, the 2 papers contradict each other, and the work preceded the age reduction in dupilumab down to 6 mo+ for AD. From a practical standpoint, as a practicing clinical immunologist who prescribes dupilumab, my anecdotal experience does not suggest any reason to withhold/alter vaccine schedules or provide ppx in any fashion for patients on dupilumab. Similarly, although I have not assessed vaccine recall in patients on drug, I have not observed adverse infectious events. Lastly, we do put patients with hyper-IgE syndrome (STAT3 LOF) with severe AD on dupilumab and do not note (small numbers obviously) adverse events to warrant avoiding this practice. • Very limited data, but no conceptual concern. • Although there does not appear to be evidence of harm, the data are insufficient to support a statement that live vaccines are safe in patients on dupilumab • Although there does not appear to be evidence of harm, the data are insufficient to support a statement that live vaccines are safe in patients on dupilumab • Case series are supportive but data is lacking
2. Patients mount appropriate antibody response to vaccines while on dupilumab.	92.9 (26)	0 (0)	• Very limit data • Based on limited data that I have seen. • There is no immunologic basis to suggest this would not be the case. • Small reduction in antibody titers in some studies but not clinically significant • I say moderate because I do not have data to support my assertion. No concerns clinically however. • Moderate evidence of low certainty supports this. • The decrease in fold change antibody titers to the COVID-19 vaccine is notable, but the COVID-19 vaccines studied are not the most robust vaccines nor a fully understood measure of immunity. The 2019 study on childhood vaccine titers is encouraging and reassuring. • Data are mixed - in some studies and for some vaccines, antibody responses are lower than in comparison group not on dupilumab; I would be cautious about using the word "appropriate" as we often do not know what level of antibody response is needed to confer immunity over a specified duration.
3. I would recommend giving live vaccines to patients on dupilumab after a shared decision-making discussion with the patient and/or their family.	89.3 (25)	3.6 (1)	• I have done this in the past • Based upon the current evidence, there have been no observations of increased harm. There are limited observations on efficacy of live vaccines in the presence of dupilumab, but this would not disfavor attempting a needed immunization. Immunizations are commonly given to patients without certainty of an immune response in the hopes of efficacy and protection. • SDM to consider possible interruption of therapy around live vaccination • The theoretical risks weighed against the basic research into IL-4's and IL-13's role in clearing viral infections as well as KO mice studies plus the clinical research data provided in the metanalysis plus the health benefit of vaccination against MMR&V tilts solidly to the side of benefit. Because of such, I would have no problem recommending live vaccination to patients receiving dupilumab in shared decision-making

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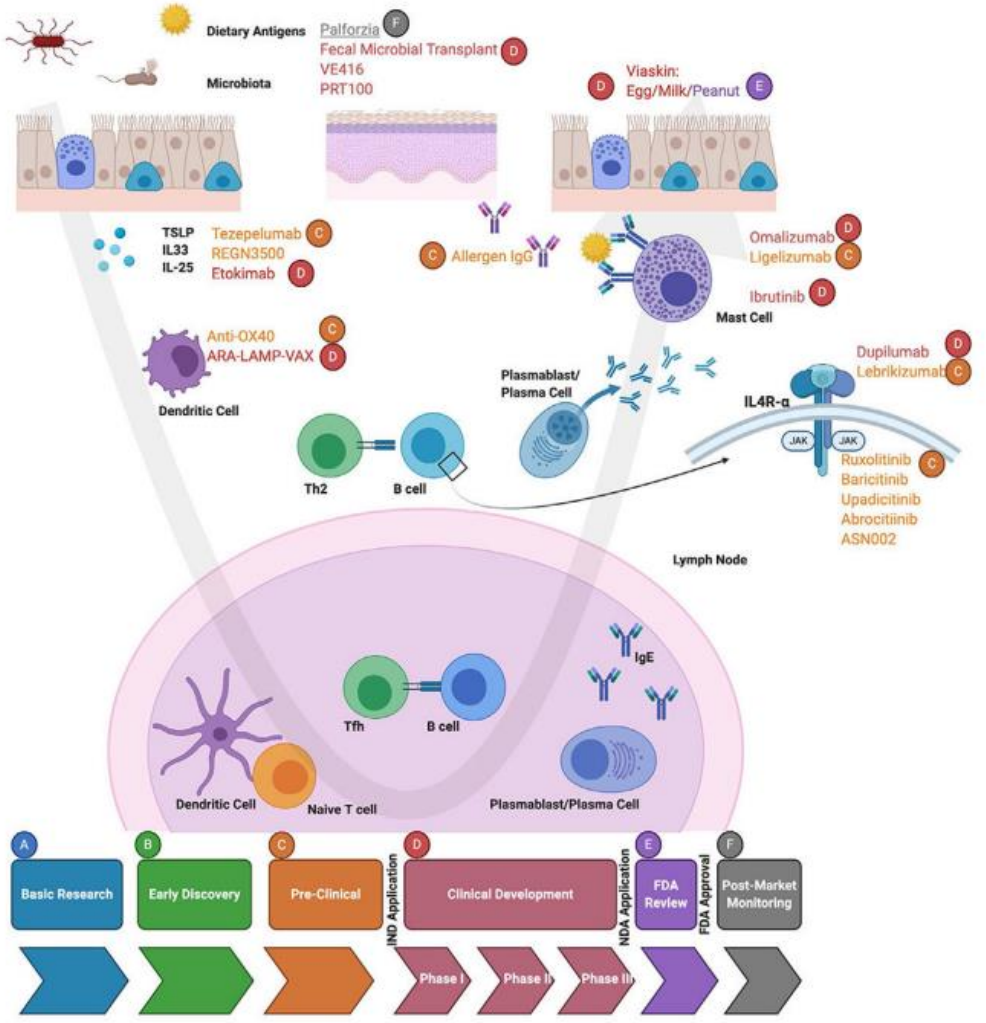
Lieberman et al. Ann All Asth Immunol 2025; 133(3): 286.

Additional Biologics



Ramsey and Berin. Ped All Immunol 2021; 32(7): 1416.

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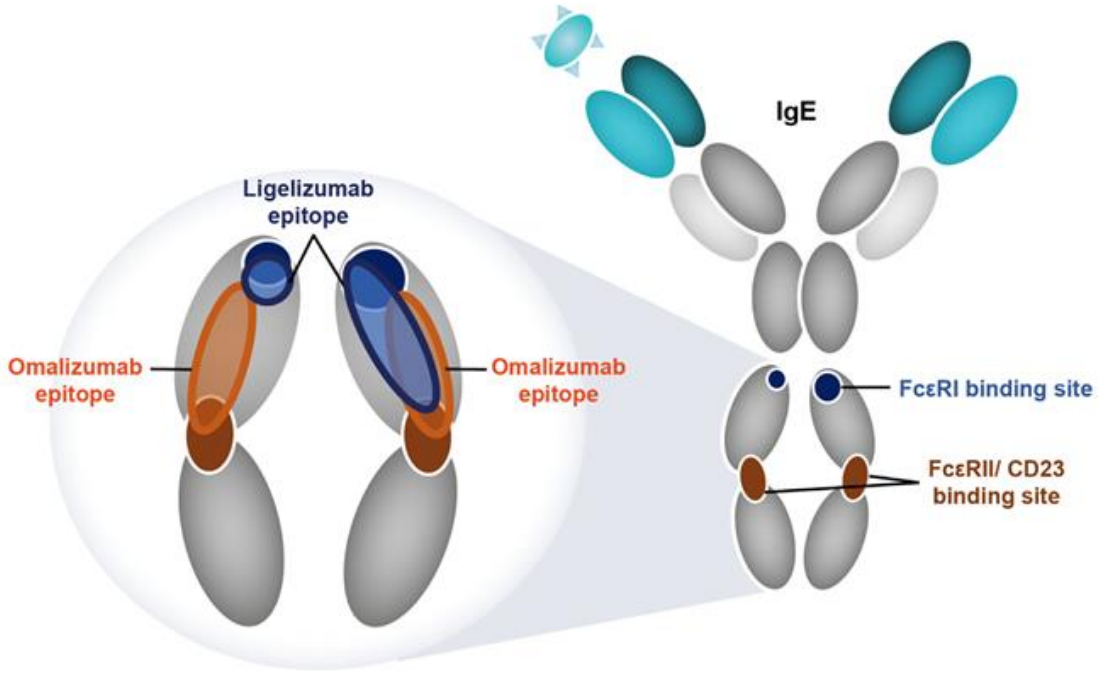
Ligelizumab



Terminated

Study terminated by sponsor

Efficacy and Safety of QGE031 (Ligelizumab) in Patients With Peanut Allergy

ClinicalTrials.gov ID NCT04984876

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Dupilumab

	Dupilumab (*N* = 24)
Male, *n* (%)	18 (75.0)
Age, years	11.7 (3.3)
Duration of peanut allergy, years	10.2 (3.1)
Age at peanut allergy diagnosis, years	1.5 (1.9)
Cumulative dose of peanut protein achieved at screening DBPCFC, mg	
Mean (SD)	10.7 (13.6)
Median (Q1, Q3)	4.0 (4.0, 14.0)
Maximum dose of peanut protein achieved at screening DBPCFC, mg	
Mean (SD)	7.5 (9.2)
Median (Q1, Q3)	3.0 (3.0, 10.0)
Total IgE, IU/ml	589.7 (499.7)
ps-IgE, kU/l	126.5 (189.4)
Skin prick test, mm	12.2 (3.8)

	Dupilumab (*N* = 24)	95% CI
Participants who passed a DBPCFC at week 24, *n* (%)		
444 mg[a]	2 (8.3)	1.03, 27.00
1044 mg[a]	0	—
Change from baseline cumulative dose (log-transformed[b]) of peanut protein achieved at week 24, mg		
Mean (SD)	0.69 (1.82)	NA
Median (Q1, Q3)	0.00 (−1.20, 1.82)	NA
Participants who passed a DBPCFC at week 36, *n* (%)	[*N* = 2][c]	
444 mg[a]	1 (50.0)	NA
1044 mg[a]	1 (50.0)	NA
2044 mg[a]	0	—

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Sindheer et al. Allergy 2025; 80(1): 227.

Summary

Considerations for Omalizumab

- Malignancy
- Anaphylaxis

Omalizumab

- Women of child bearing age
- Immunosuppression

Future Biologics

- Failed trials
- Multiple targets to explore

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Thank You

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