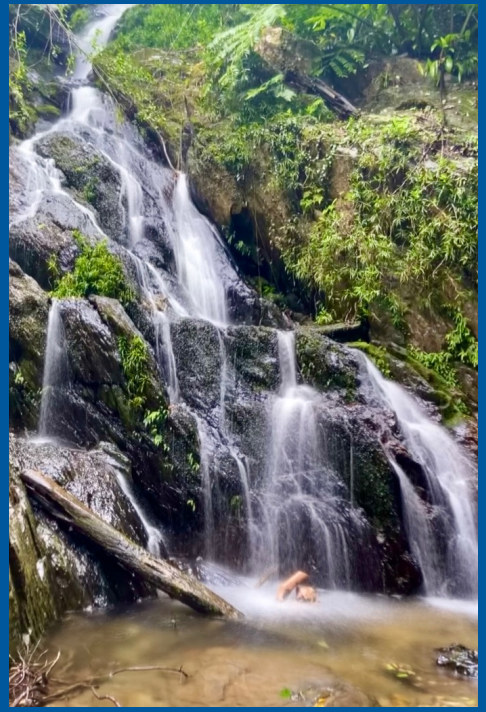
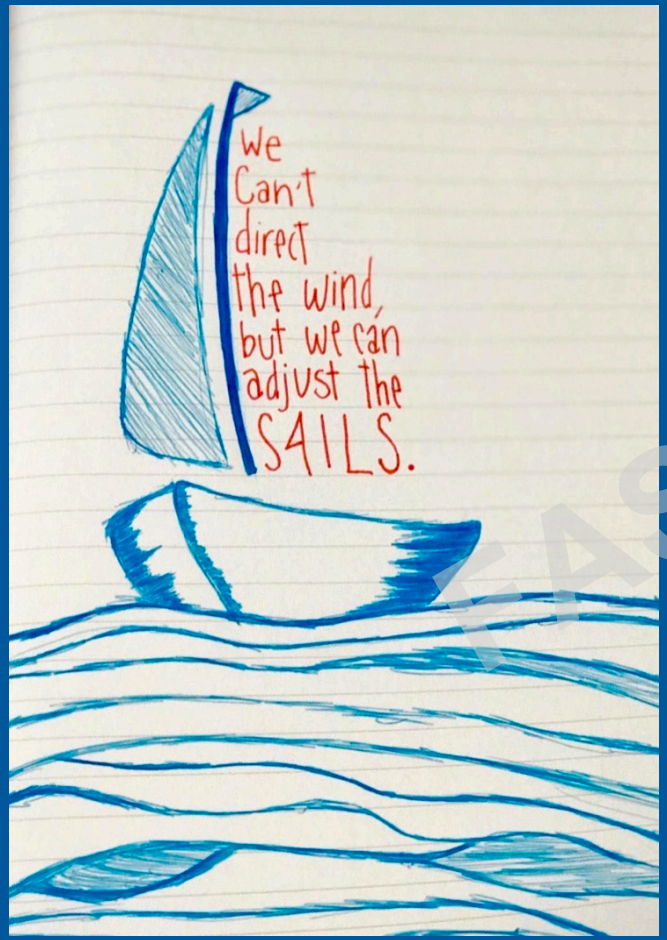


Practical use of biologics

FOOD ALLERGY SUPPORT TEAM
Tackling Food Allergies Together

Douglas Jones, MD, FAAAAI, FACAAI

FAST June 22, 2024



Objectives

Right patient, right treatment, right time

- **Review**
  Current FDA indication of omalizumab
- **Discuss other possibilities**
  Why consider it? How to utilize it?
- **Consider other biologics**
  How they may help some who could not previously consider treatment, now be a candidate

OUtMATCH STUDY SUMMARY

SCREENING

Oral Food Challenges x 4
(Placebo, Peanut, and 2 Other Food Allergens) up to 4 weeks

2 or 3 additional Oral Food Challenges (Placebo and 1 or 2 Other Food Allergens) up to 2-3 weeks may be needed

PASS

FAIL

STOP

STAGE 1

1. Omalizumab or Placebo
given as an injection every 2 or 4 weeks for 16-20 weeks

2. Oral Food Challenges x 4
(Placebo and 3 Food Allergens) up to 4 weeks

Participants 1-60

Participants 61-225

STAGE 1 OPEN-LABEL EXTENSION

1. Omalizumab given as an injection every 2 or 4 weeks for 24-28 weeks

2. Oral Food Challenges x 4
(Placebo and 3 Food Allergens) up to 4 weeks

3. Continue to STAGE 3

Length of Stage 1: 4 to 5 months
Length of Stage 1 Open-Label Extension: 6 to 7 months

STAGE 2

1. **Omalizumab** given as an injection every 2 or 4 weeks for 8 weeks

Placed on either

2a. Multi-Allergen OIT* and continued **Omalizumab** injections for 8 weeks

3a. Continue **Multi-Allergen OIT***, now with **Placebo** injections for 44 weeks

2b. Placebo OIT* and continued **Omalizumab** injections for 8 weeks

3b. Continue **Placebo OIT*** and **Omalizumab** injections for 44 weeks

If you react to the lowest dose during initial dose escalation or you can not reach the maintenance dose within 24 weeks, you will be removed from the study.

4. Oral Food Challenges x 4
(Placebo and 3 Food Allergens) up to 4 weeks

5. Continue to STAGE 3

Length of Stage 2: 14 to 15 months

* OIT - Oral Immunotherapy

STAGE 3

Using the results of the Stage 2 or Stage 1 Open-Label Extension Oral Food Challenges, go on 1 of the following 3 plans for each food:

Diet Plan

Eat food in clinic

Add food to diet

Diet Plan or Rescue OIT Plan

Rescue OIT Plan for 52 weeks

Oral Food Challenge to Food

Diet Plan or Food Avoidance Plan

Food Avoidance Plan

Followed until December 2023

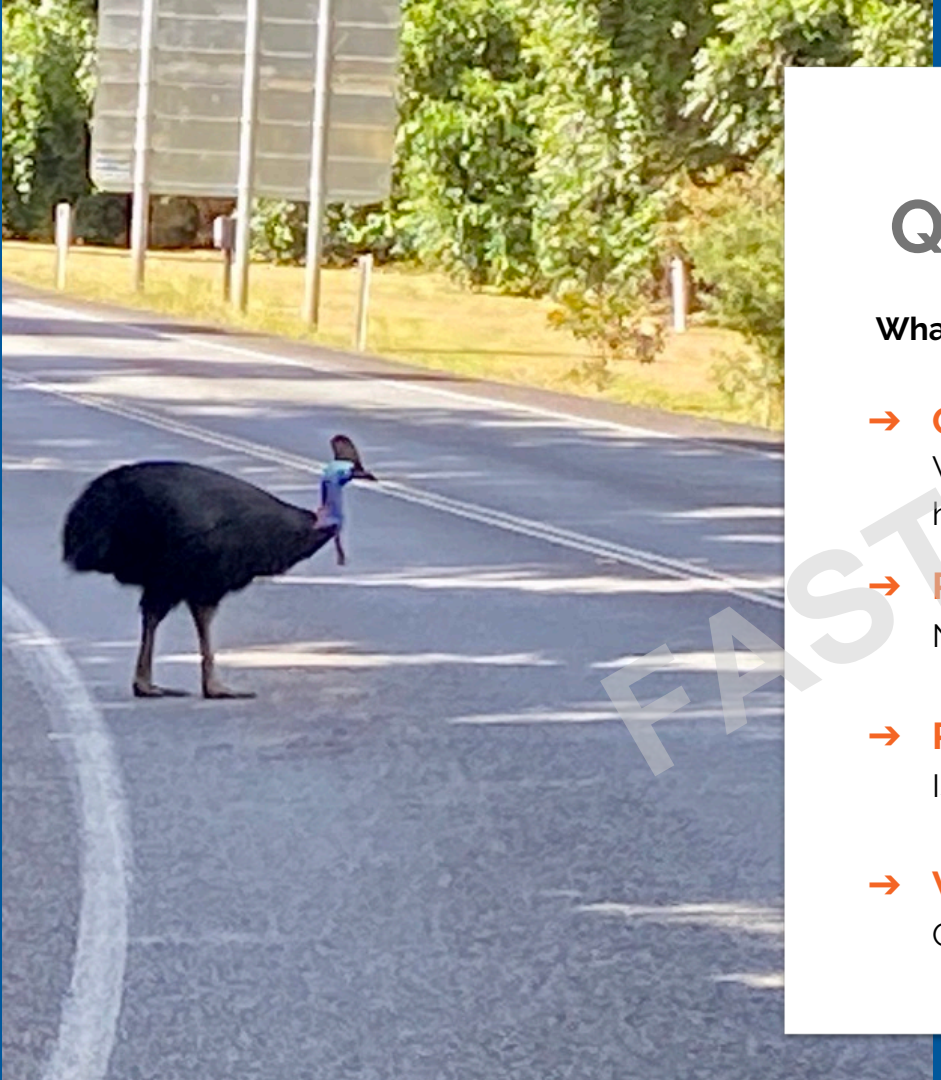
Keys of Indication

OUtMATCH Stage 1

XOLAIR is indicated for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatrics patients aged 1 year and older with IgE-mediated food allergy.

XOLAIR is to be used in conjunction with food allergen avoidance.

Limitations of Use: XOLAIR is not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

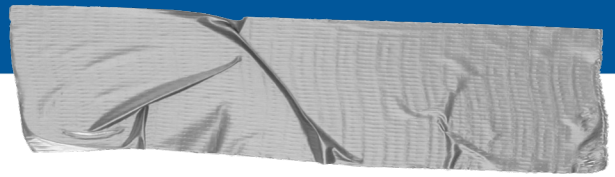


Questions/Objections

What do patients ask and what do you need to consider?

- **Cost**
  What is the cost going to be for the patient and the health care system?
- **Recurrent injection**
  Need to consider with young children especially
- **Risks**
  Is the Risk:Benefit worth it?
- **Will it really work and how will I know?**
  Given the data…

How Risks Compare to Avoidance



Key aspects

Anaphylaxis with omalizumab:
In premarketing clinical trials, anaphylaxis was reported in 3 of 3507 (0.1%) patients

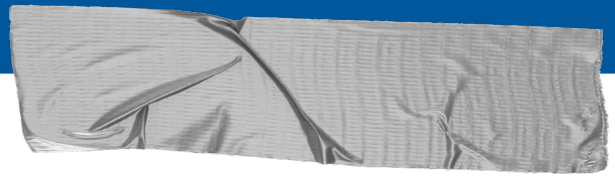
In post-marketing reports, the frequency of ANA was ~0.2% of patients based on an estimated exposure of about 57,300 patients from June 2003 through December 2006

Anaphylaxis with avoidance and accidental exposures:
A study published in JACI found that ~11.5% of FA patients experienced at least one accidental exposure over a 2-year period

Research in Pediatrics found ~14.3% of FA children had experienced an accidental exposure in the previous year

Another study from Clinical and Experimental Allergy showed up to 55% of FA children had accidental exposures over a 3-year period.

Risks Of Malignancy



Key aspects

Malignancy:
Malignant neoplasms were observed in 20 of 4127 (0.5%) XOLAIR-treated patients compared with 5 of 2236 (0.2%) control patients in clinical studies of adults and adolescents (≥12 years of age) for a different indication and other allergic disorders.

A subsequent 5-year observational study of 5007 XOLAIR-treated and 2829 non-XOLAIR-treated adolescent and adult patients for a different indication found that the incidence rates of primary malignancies (per 1000 patient years) were similar in both groups (12.3 vs 13.0, respectively)

****This has not been assessed in children**

Dosing is similar but different than asthma

ADMINISTER XOLAIR BY SUBCUTANEOUS INJECTION EVERY 2 OR 4 WEEKS

Pretreatment Serum IgE (IU/mL)	Dosing Frequency	Body Weight (kg) Dose (mg)												
		≥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
≥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

■ Subcutaneous doses to be administered every 4 weeks ■ Subcutaneous doses to be administered every 2 weeks

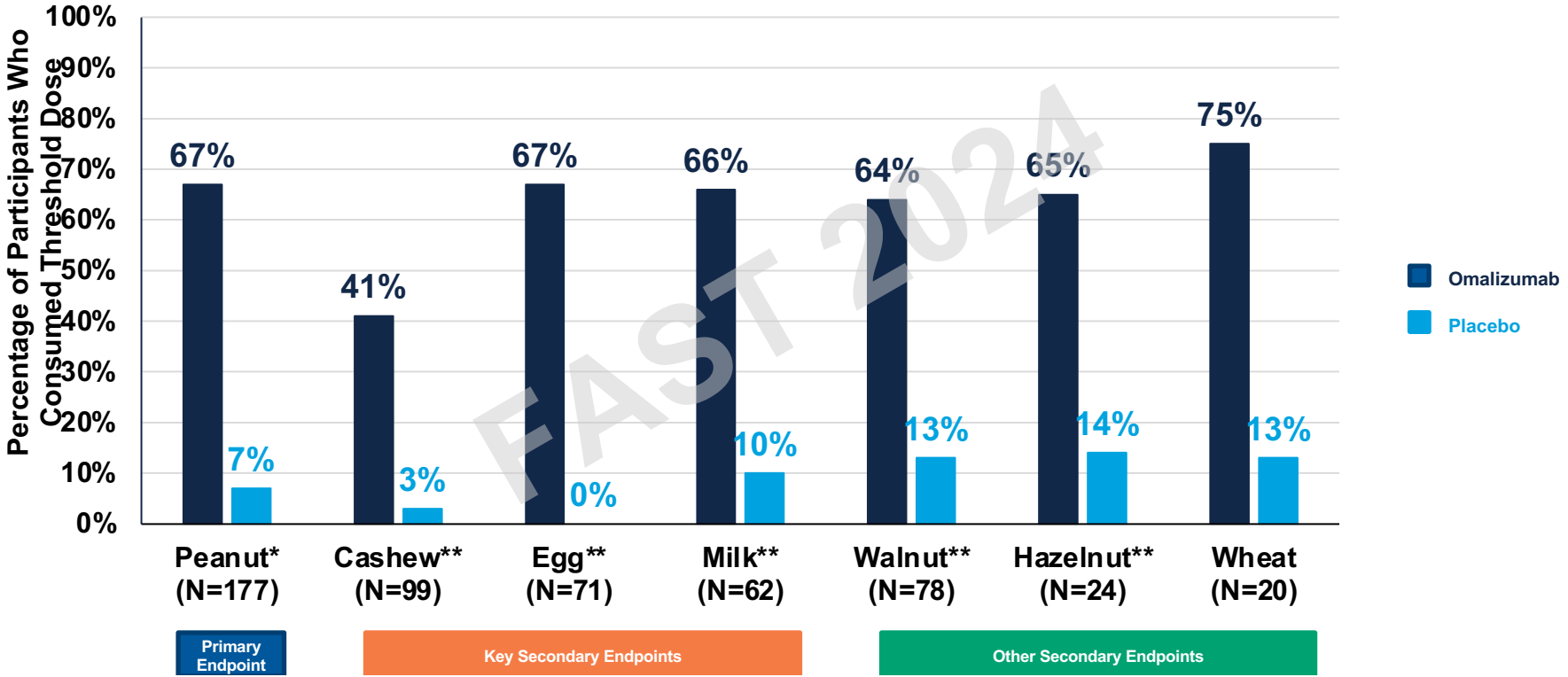
IgE=immunoglobulin E.

Reference: XOLAIR [prescribing information]. Genentech USA, Inc. and Novartis Pharmaceuticals Corporation.

Will it work **AND**
How will I know?

OUtMATCH Stage 1 and OLE Final Analysis (N=180)

PRIMARY AND SECONDARY ENDPOINT RESULTS



Note: *Up to a dose of 600 mg of peanut protein for a maximum cumulative dose of 1,044 mg. **Dose of up to 1000 mg of food protein for a maximum cumulative dose of 2,044 mg.

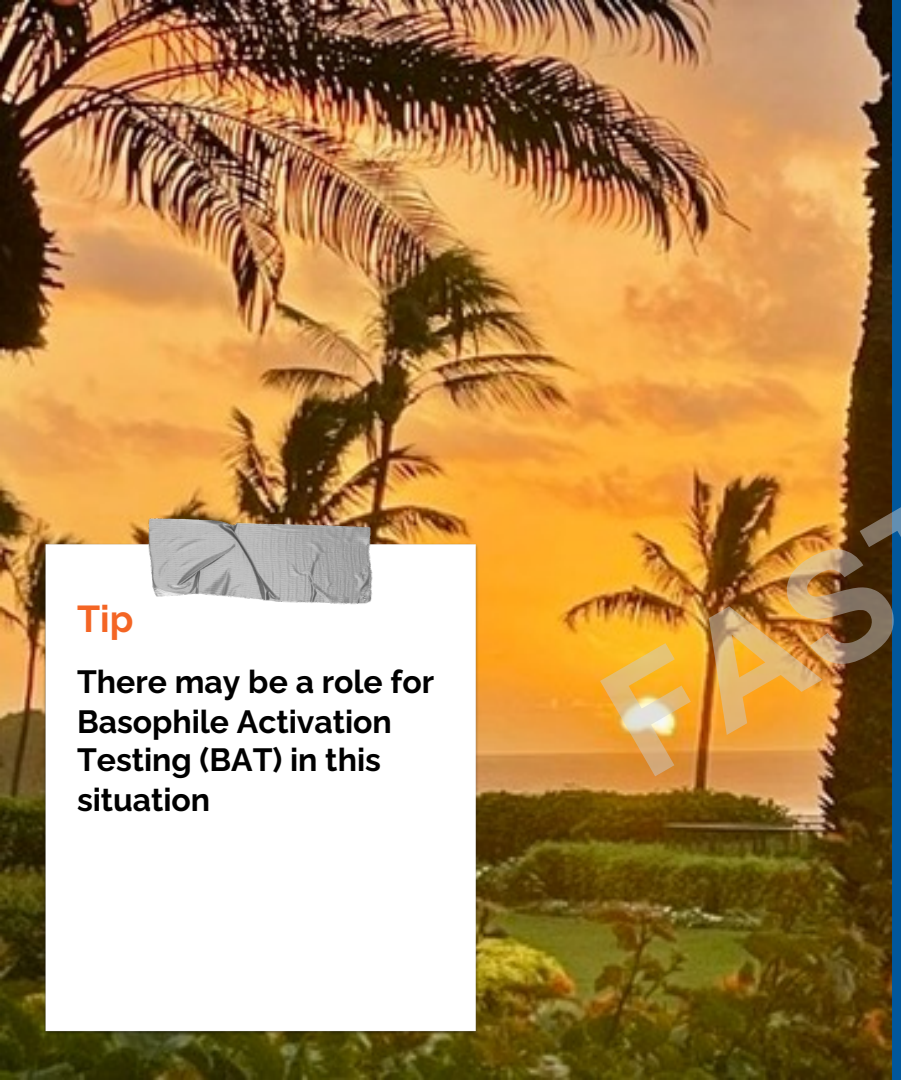
Reference: Wood et al. N Engl J Med 2024. Figure 1.

Open-label extension study

The first 60 patients (59 pediatric and one adult) who completed the double-blind, placebo-controlled phase of the study could continue into the Open Label Extension (OLE)

Of these, 38 pediatric patients who received Xolair continued on Xolair for 24 to 28 weeks in OLE. While efficacy cannot be established from uncontrolled, open-label studies, the percentage of patients who were able to tolerate protein levels set for primary (≥600 mg) and secondary endpoints (≥1000 mg) was maintained.[1]

Reference: XOLAIR [prescribing information]. Genentech USA, Inc. and Novartis Pharmaceuticals Corporation.



Tip

There may be a role for Basophile Activation Testing (BAT) in this situation

What do we do?

I suggest we do what allergists are trained to do when food allergy status is in doubt…**Challenge**

How to challenge and when?

DOSING SCHEDULE FOR DBPCFCS: OUTMATCH

	Baseline*		Stage 1		Open-label Extension	
Dose #	**Food Protein/ Placebo (mg)**	**Cumulative Dose (mg)**	**Food Protein/ Placebo (mg)**	**Cumulative Dose (mg)**	**Food Protein/ Placebo (mg)**	**Cumulative Dose (mg)**
1	1	1	1	1	1	1
2	3	4	3	4	3	4
3	10	14	10	14	10	14
4	30	44	30	44	30	44
5	100	144	100	144	100	144
6	300†	444	300	444	300	444
7			600	1044	600	1044
8			1000	2044	1000	2044
9			2000 [Dose 1]	4044	2000 [Dose 1]	4044
10			2000 [Dose 2]	6044	2000 [Dose 2]	6044
11					2000 [Dose 3]	8044

*Baseline=Screening.

†During the double-blind, placebo-controlled food challenge to peanut at Baseline, the 300 mg dose was actually placebo to preserve blinding and to not surpass a maximum dose of 100 mg of peanut protein.

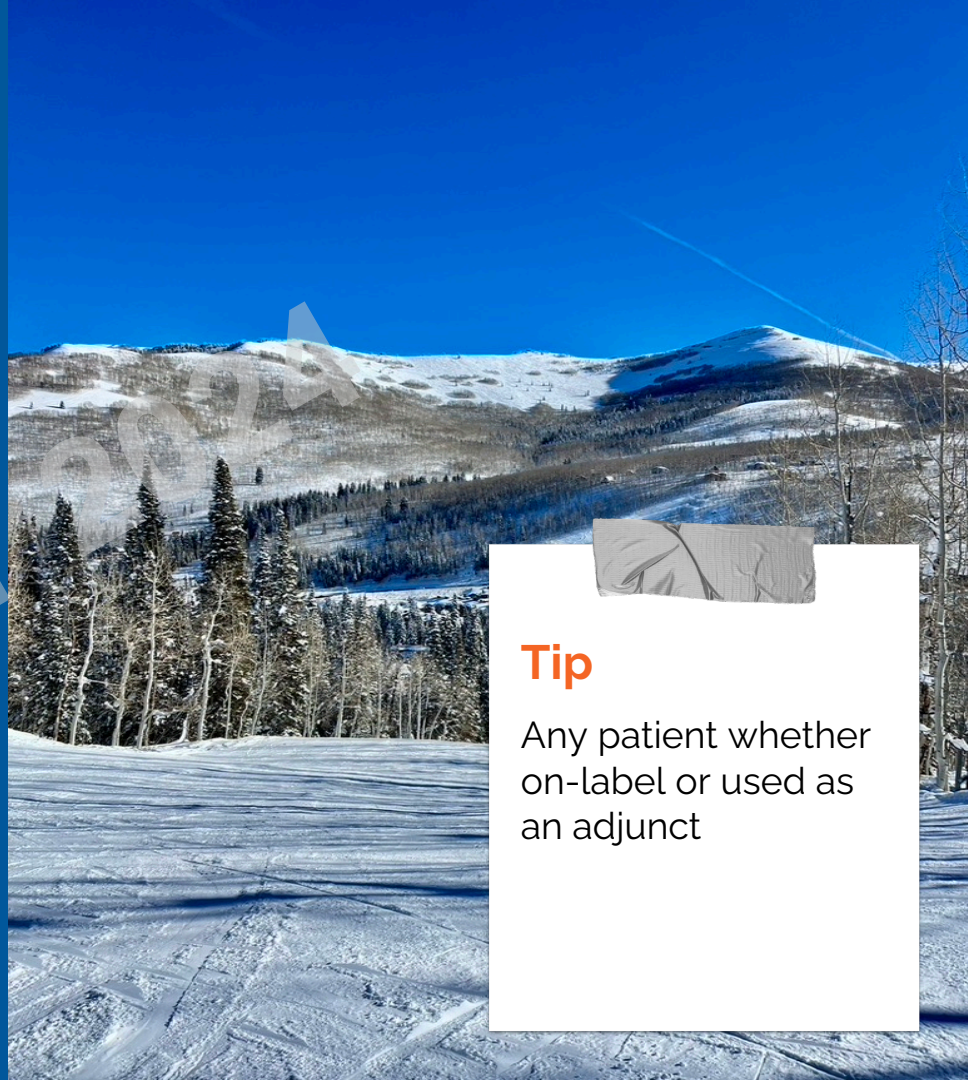
All food challenges were double-blind, placebo-controlled.

How to challenge in the real world?

Patient Considerations for ”on-label use”

- Anxiety
- Asthmatics
- Travel
- Label reading
- For those not ready for OIT/SLIT
- Adults

Story for illustration purposes only

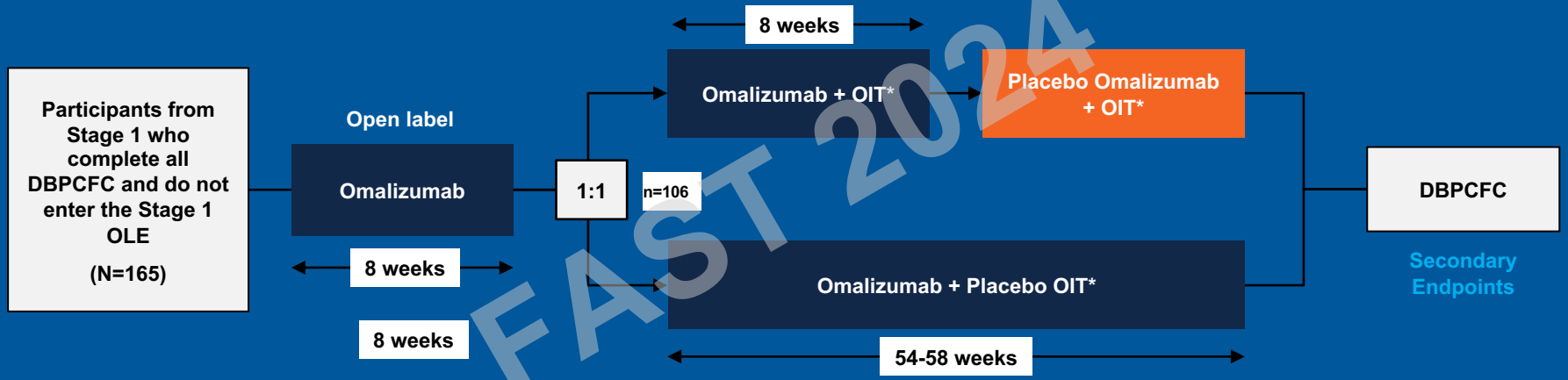


Tip

Any patient whether on-label or used as an adjunct

OUtMATCH STAGE 2

Stage 2 evaluates how a short course of omalizumab combined with multiallergen OIT compares with a longer course of omalizumab in decreasing allergic reactions



Secondary Endpoints

Number of participants who successfully consume ≥**1 dose of 2000 mg protein of all 3 foods** without dose-limiting symptoms during the DBPCFC at the end of Stage 2

Notes: *OIT will be multifood.
Abbreviations: DBPCFC=double-blind, placebo-controlled food challenge; OIT=oral immunotherapy; OLE=open-label extension.
Reference: Clinicaltrials.gov https://clinicaltrials.gov/ct2/show/NCT03881696. Accessed January 11, 2022.

Bégin et al. Allergy, Asthma & Clinical Immunology 2014, 10:7
http://www.aacijournal.com/content/10/1/7

RESEARCH

Phase 1 results of safety and tolerability i oral immunotherapy protocol to multiple using Omalizumab

Philippe Bégin[1], Tina Dominguez[1], Shruti P Wilson[1], Liane Bacal[1], Anjuli Mehrotra[1], Bethany Kausch
Morvarid Tavassoli[1], Elisabeth Hoyte[1], Gerri O'Riordan[1], Alanna Blakemore[1], Scott Seki[1], Robert G H...
and Kari C Nad...[1*]

Original Article

Omalizumab in IgE-Mediated Food Allergy: A Systematic Review and Meta-Analysis

Torsten Zuberbier, PhD[a,b], Robert A. Wood, MD[c], Carsten Bindslev-Jensen, PhD[d,e], Alessandro Fiocchi, MD[f], R. Sharon Chinthrajah, MD[g,h], Margitta Worm, MD[i], Antoine Dos... MD[j], Montserrat Fernandez-Rivas, PhD[k], Alexandra F. Santos, PhD[l,m,n,o], Xavier Jaumont, MD[p], a...
Denmark; Rome, Italy; Stanford, Calif; Lille, France; Madrid, ...

CONCLUSIONS: In IgE-mediated food allergy, OMA can help patients consume multiple foods and allow for food dose escalation. As an adjunct to OIT, OMA can also support high-dose desensitization and higher maintenance doses. Further studies are warranted to empirically evaluate the effect of OMA and confirm these findings. (J Allergy Clin Immunol Pract 2023;11:1134-46)

Food, drug, insect sting allergy, and anaphylaxis

A pilot study of omalizumab to facilitate rapid oral desensitization in high-risk peanut-allergic patients

Lynda C. Schneider, MD,* Rima Rachid, MD,* Jennifer LeBovidge, PhD, Emily Blood, PhD, Mudita Mit
Dale T. Umetsu, MD, PhD *Boston, Mass*

Published in
J Allergy ...

Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy

Kari C. Nadeau, MD, PhD[b], Lynda C. Schneider, MD[a], Lisa Hoyte, NP[b], Irene Borras, NP[a], and Dale T. Umetsu, MD, PhD[a]

[a]Division of Immunology, Children's Hospital, Harvard Medical School, Boston, Mass

[b]the Division of Immunology and Allergy, Department of Pediatrics, Stanford University, Calif.

Omalizumab facilitates rapid oral desensitization for peanut allergy

Andrew J. MacGinnitie, MD, PhD,[a]* Rima Rachid, MD,[a]* Hana Gragg, MPH,[b] Sara V. Little, BA,[a] Paul Lakin, MS,[b] Antonella Cianferoni, MD,[c] Jennifer Heimall, MD,[c] Melanie Makhija, MD,[d] Rachel Robison, MD,[d] R. Sharon Chinthrajah, MD,[e] John Lee, MD,[a] Jennifer Lebovidge, PhD,[a] Tina Dominguez, PA,[e] Courtney Rooney, RN,[c] Megan Ott Lewis, MSN, CRNP,[c] Jennifer Koss, RN,[d] Elizabeth Burke-Roberts, MSN, CPNP,[a] Kimberly Chin, BA,[b] Tanya Logvinenko, PhD,[b] Jacqueline A. Pongracic, MD,[d] Dale T. Umetsu, MD, PhD,[f]‡ Jonathan Spergel, MD, PhD,[c]‡ Kari C. Nadeau, MD, PhD,[e]‡ and Lynda C. Schneider, MD[a]‡ *Boston, Mass, Philadelphia, Pa, Chicago, Ill, and Palo Alto and South San Francisco, Calif*

Background: Peanut oral immunotherapy is a promising approach to peanut allergy, but reactions are frequent, and some patients cannot be desensitized. The anti-IgE medication omalizumab (Xolair; Genentech, South San Francisco, Calif) might allow more rapid peanut updosing and decrease reactions.
Objective: We sought to evaluate whether omalizumab facilitated rapid peanut desensitization in highly allergic patients.
Methods: Thirty-seven subjects were randomized to omalizumab (n = 29) or placebo (n = 8). After 12 weeks of treatment, subjects underwent a rapid 1-day desensitization of up to 250 mg of peanut protein, followed by weekly increases up to 2000 mg. Omalizumab was then discontinued, and subjects continued on 2000 mg of peanut protein. Subjects underwent an open challenge to 4000 mg of peanut protein 12 weeks after stopping study drug. If tolerated, subjects continued on 4000 mg of peanut protein daily.
Results: The median peanut dose tolerated on the initial desensitization day was 250 mg for omalizumab-treated subjects versus 22.5 mg for placebo-treated subject. Subsequently, 23 (79%) of 29 subjects randomized to omalizumab tolerated 2000 mg of peanut protein 6 weeks after stopping omalizumab versus 1 (12%) of 8 receiving placebo ($P < .01$). Twenty-three subjects receiving omalizumab versus 1 subject receiving placebo passed the 4000-mg food challenge. Overall reaction rates were not significantly lower in omalizumab-treated versus placebo-treated subjects (odds ratio, 0.57; $P = .15$), although omalizumab-treated subjects were exposed to much higher peanut doses.
Conclusion: Omalizumab allows subjects with peanut allergy to be rapidly desensitized over as little as 8 weeks of peanut oral immunotherapy. In the majority of subjects, this desensitization is sustained after omalizumab is discontinued. Additional studies will help clarify which patients would benefit most from this approach. (J Allergy Clin Immunol 2017;139:873-81.)

Key words: *Peanut allergy, food allergy, desensitization, omalizumab*

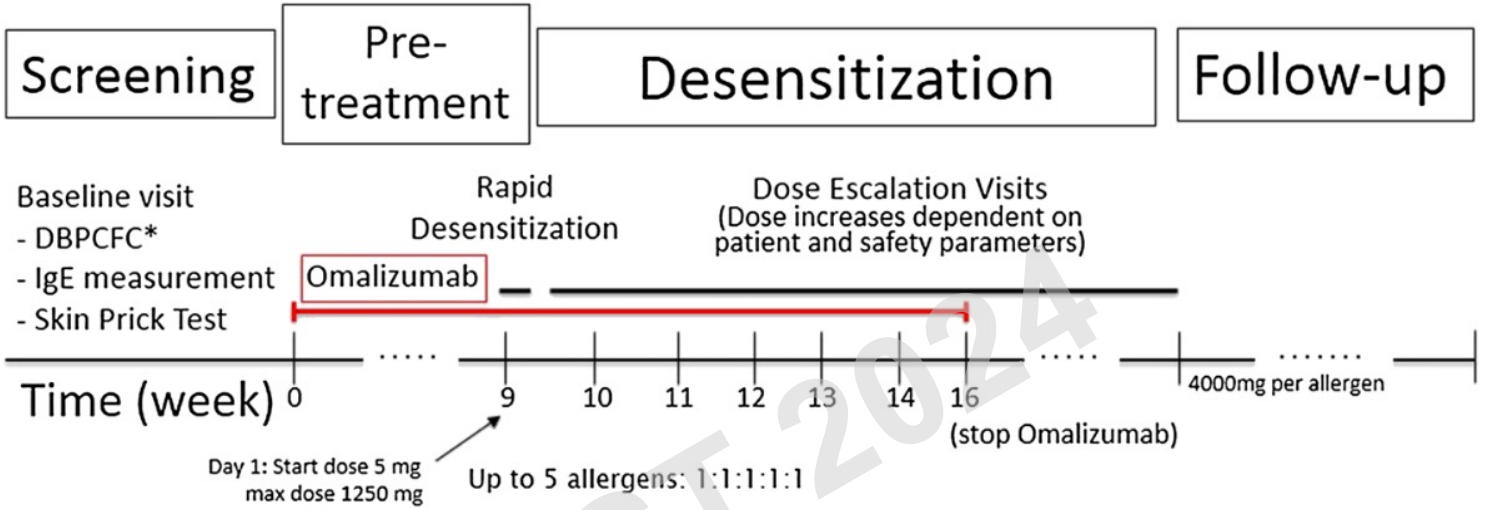


Table 1 Rush mOIT initial escalation day schedule

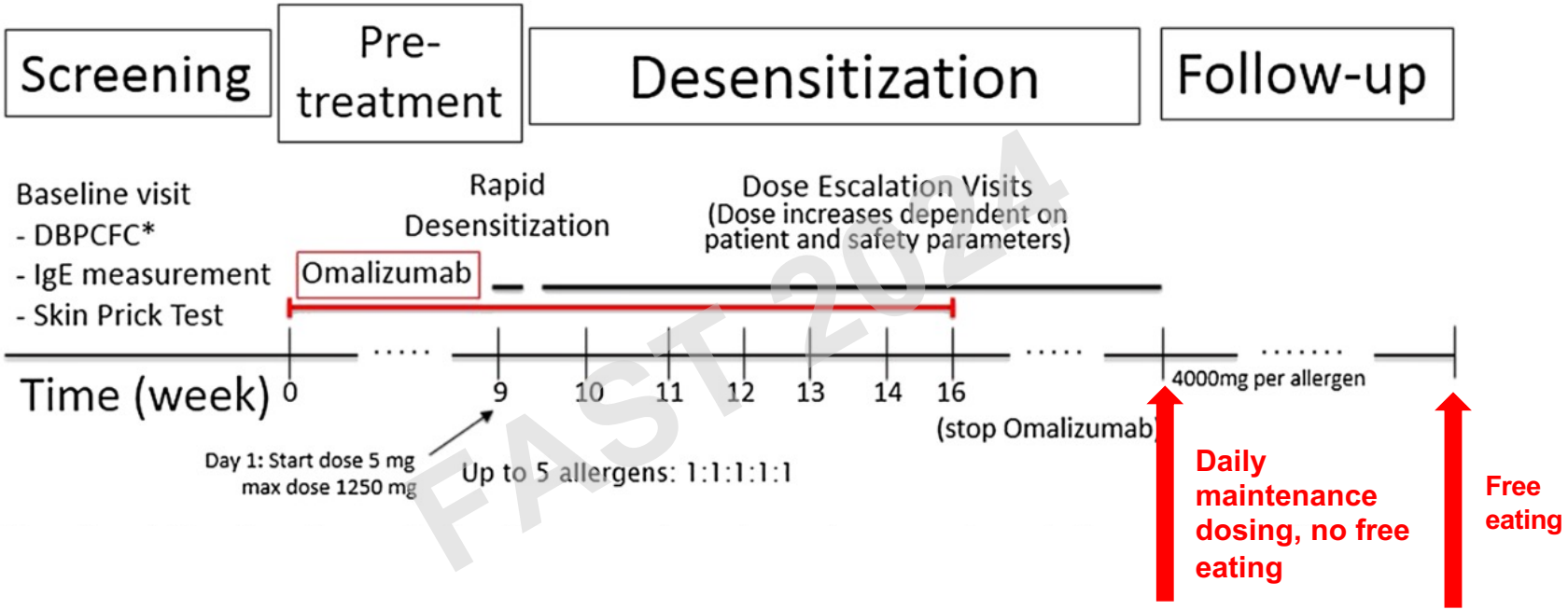
Dose in mg of protein	Dosing interval in minutes
5	30
50	30
150	30
300	30
625	30
1250	120

Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using Omalizumab

Philippe Bégin[1], Tina Dominguez[1], Shruti P Wilson[1], Liane Bacal[1], Anjuli Mehrotra[1], Bethany Kausch[1], Anthony Trela[1], Morvarid Tavassoli[1], Elisabeth Hoyte[1], Gerri O'Riordan[1], Alanna Blakemore[1], Scott Sek[1], Robert G Hamilton[2] and Kari C Nadeau[1*]

Table 2 Rush mOIT dose escalation schedule

Dose of protein (mg)	Interval in weeks	% of increase from previous
2350 mg	2	88%
4000 mg	2	70%
5800 mg	2	45%
7600 mg	2	50%
9400 mg	2	30%
11200 mg	2	20%
14000 mg	2	25%
17500 mg	2	25%
20000 mg	2	14%



- Total 24 weeks of omalizumab as opposed to 16.
- 2 challenges: one on omalizumab and the second after a washout

Stop omalizumab at week 24 prior to final challenge

2nd challenge after washout

Day 1 and updosing protocol

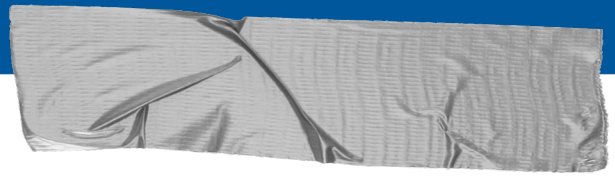
Rush OIT day 1 schedule with omalizumab. Per food

Dose in mg of protein	Dose interval
1mg	30
10mg	30
30mg	30
60mg	30
125mg	30
250mg	120

Rush OIT dose escalation schedule

Dose in mg of protein	Interval in weeks	% of increase from previous
470mg	2	88%
800mg	2	70%
1160mg	2	45%
1520mg	2	50%
1880mg	2	30%
2240mg	2	20%
2800mg	2	25%
3500mg	2	25%
4000mg	2	14%
8000mg final challenge (last dose of omalizumab within 48 hours prior)	6-8 weeks	Maintenance dosing daily with no extras while omalizumab washes out
8000mg final challenge	Done	Omalizumab washed out

Omalizumab as OIT adjunct Why?



Key Aspects

What do you need to consider?

Cost

Fixed as opposed to indefinite
Bio-similar's on the way

Patient considerations

Adults
Shrimp
Salvage
Extenuating circumstances
Make treatment a reality for some who would not consider it otherwise

Is this the sweet spot?

Desensitization, freedom, speed, efficacy, safety, and reduction of side effects?

Other Biologics +/- Comorbidities

Key Aspects

What do you need to consider?

Previous absolute or relative contraindications or poses higher risk to patients

Severe asthma
Severe eczema
Severe anxiety
EoE
MCAS
CSU

Utilize to shift from contraindication to feasible

If no co-morbidities: Omalizumab > Others

Build the bridge

Meet patients where they are and lead them to where THEY want to go—build the bridge for them

Right patient, right treatment, right time

slido

Please download and install the Slido app on all computers you use

24. Do you intend to use Xolair in your practice?

ⓘ Start presenting to display the poll results on this slide.

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25. If you will use Xolair, will you do oral food challenges after a few months to see if it is working?

ⓘ Start presenting to display the poll results on this slide.

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Please download and install the Slido app on all computers you use

26. For those who will challenge, how will you do it?

ⓘ Start presenting to display the poll results on this slide.

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