



*Oral Immunotherapy and Anti-IgE Antibody-
Adjunctive Treatment for Food Allergy:
Omalizumab facilitates oral desensitization in high-risk
peanut allergy patients*

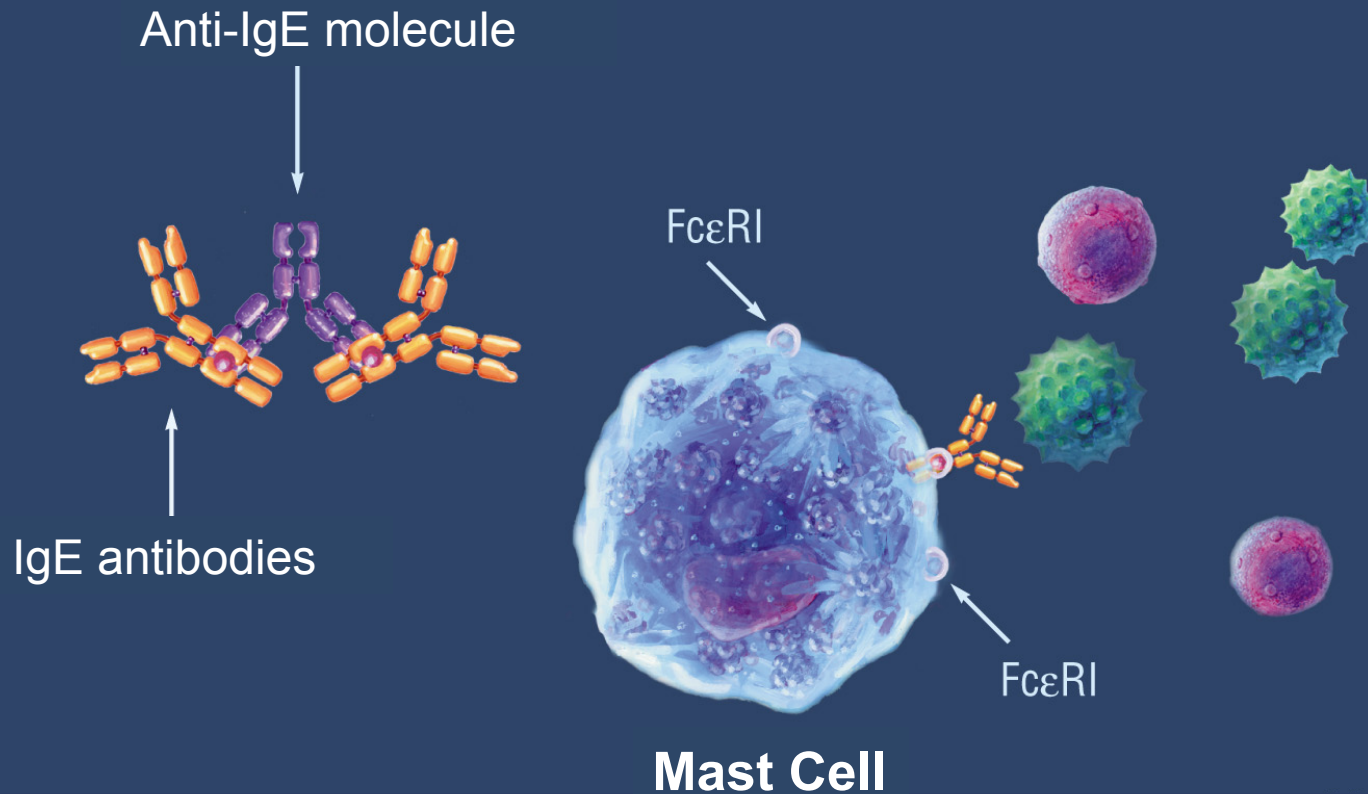
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Oral food immunotherapy/desensitization

- OIT for food allergy has been studied for many years.
 - Based on allergen immunotherapy for hay fever— allergy shots.
 - Oral food desensitization works.
 - However, allergic reactions, including anaphylaxis, are very common, and 10-25% of patients have severe reactions, and are refractory to desensitization.
 - Children with higher food-specific IgE are more likely to fail desensitization (Meglio et al 2013. *Pediatr Allergy Immunol.*)

Can anti-IgE Antibody be used for food allergy?

Anti-IgE Antibody (omalizumab)



- Anti-IgE binds IgE and prevents mast cell degranulation.
- Reduces expression of Fc ϵ R1 on mast cells and basophils.
- Circulating anti-IgE complexes act as antigen sink.
- Possible effects on DCs and monocytes, which express Fc ϵ R1.

Can omalizumab be used in food allergy?

- Anti-IgE increased the threshold dose of peanut eliciting a clinical reaction.
 - TNX-901 (450 mg x 4 doses) increased the tolerated dose from 178 to 2,800 mg peanut flour (Leung et al. 2003. NEJM).
 - Omalizumab increased the tolerated dose of peanut from a median of 15 to 500 mg flour (Sampson et al. 2011. JACI) or 80 to 6,500 mg (Savage et al. 2012. JACI).
- Anti-IgE pretreatment decreases acute reactions during rush immunotherapy for ragweed allergy (Casale et al. 2006. JACI).

Can omalizumab make oral immunotherapy faster and more effective?

- Subjects (Boston & Stanford) with significant milk allergy:
 - 11 children, 7-18 years of age.
 - Median Milk-specific IgE was 50 kU/L.
- Treatment protocol:
 - Receive omalizumab for 16 weeks.
 - During the last 7 wks of omalizumab, patients received milk, starting at a very low dose, which increased 20,000-fold.
 - Omalizumab was then stopped, but the patients continued on daily oral milk.
 - At 25 wks, oral food challenge, >8 oz of milk.

Overall Results, milk study

- One-day desensitization to 1 oz of milk.
 - **7 out of 11 patients passed.**
 - **One patient dropped out after first day of desensitization.**
- After 7 additional weeks, tolerated a daily dose of 2 oz.
 - **9 out of 10 patients passed.**
- At 6 months, oral challenge, total of 11 oz milk).
 - **9 out of 10 patients passed.**
 - **The 10th patients was taking 4 ounces of milk or milk products daily.**

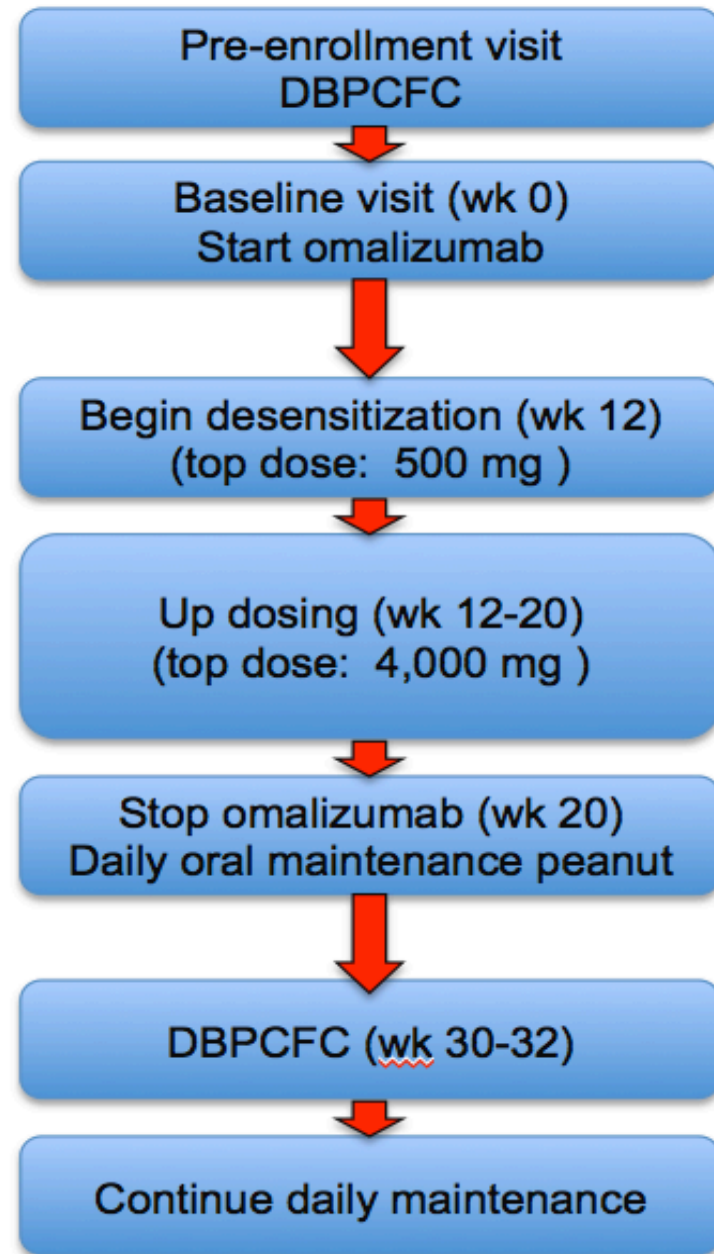
After the Milk Study, what's next?

- Follow the milk-desensitized patients for at least 2 more years.
 - Make sure they remain tolerant of milk.
 - Determine if tolerance improves with time.
 - Examine the immune system for changes.
 - Will they still need daily milk to maintain tolerance?
- **Can we use this approach for other foods?**

Will Xolair Facilitate Desensitization of Peanut Allergic Patients?

- Recruitment:
 - Patients 7-25 years of age: 13 patients, median age, 10 y.
 - History of severe peanut allergy.
 - Median peanut specific IgE, 229 kU_A/L (highest of any study).
 - All patients reacted on challenge with a median dose of 50 mg peanut flour (about ¼ peanut).
- Treatment:
 - Xolair for a total of 20 weeks.
 - Desensitization over 8 weeks, starting at 0.1 mg of peanut, and increasing 40,000-fold to 4,000 mg (about 10 peanuts).
 - The Xolair was then stopped, but the children continued on daily oral peanuts.
 - 12 weeks later, oral food challenge.

- Treatment:
 - Xolair every 2-4 weeks.
 - Desensitization, over 8 weeks, starting at 0.1 mg of peanut, and increasing 40,000-fold to 4,000 mg (about 11 peanuts).
 - After stopping Xolair, continue daily peanuts.
 - 12 weeks later, oral food challenge.



Comparison to Previous Studies

- Our patients had the highest median peanut specific IgE.
- One day desensitization to 500 mg.
 - In our study, 13 of 13 patients were successful.
 - S. Jones: 10 of 39 tolerated 200 mg.
 - Hofmann: 6 of 28 subjects tolerated 200 mg.
- With omalizumab treatment, patients required a median time of 8 wks to reach maintenance.
- Without omalizumab, median time to reach maintenance: 20-30 wks.

Summary

- Among children with significant milk allergy, treatment with Xolair facilitated rapid oral desensitization.
- Among children with high-risk peanut allergy, treatment with Xolair facilitated rapid oral desensitization.
- The majority of peanut allergic patients were successfully desensitized with Xolair pretreatment and are now taking 10 or more peanuts per day!
- Patients still need to be followed, as reactions can still occasionally occur with oral doses.

Limitations

- Small samples size.
- Absence of a placebo group.

What's next?

- Follow the patients over an additional 3-5 years.
- Validate results with larger studies.
- PRROTECT study.
 - Four site study
 - Boston Children's Hospital (Schneider)
 - Children's Hospital of Philadelphia (Spergel)
 - Lurie Children's Hospital Chicago (Pongratic)
 - Stanford University (Nadeau)
 - 36 patients.
 - Funded by FARE and Genentech.

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